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Association of Ventilation Rates and CO_2 Concentrations with Health and Other Responses in Commercial and Institutional Buildings

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Abstract This paper reviews current literature on the associations of ventilation rates and carbon dioxide concentrations in non-residential and non-industrial buildings (primarily offices) with health and other human outcomes. Twenty studies, with close to 30,000 subjects, investigated the association of ventilation rates with human responses, and 21 studies, with over 30,000 subjects, investigated the association of carbon dioxide concentration with these responses. Almost all studies found that ventilation rates below 10 Ls^{-1} per person in all building types were associated with statistically significant worsening in one or more health or perceived air quality outcomes. Some studies determined that increases in ventilation rates above 10 Ls^{-1} per person, up to approximately 20 Ls^{-1} per person, were associated with further significant decreases in the prevalence of sick building syndrome (SBS) symptoms or with further significant improvements in perceived air quality. The carbon dioxide studies support these findings. About half of the carbon dioxide studies suggest that the risk of sick building syndrome symptoms continued to decrease significantly with decreasing carbon dioxide concentrations below 800 ppm. The ventilation studies reported relative risks of 1.5–2 for respiratory illnesses and 1.1–6 for sick building syndrome symptoms for low compared to high low ventilation rates.

Key words Ventilation rates; Carbon dioxide; Health effects; SBS symptoms; Air exchange rate; Relative risks.

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Introduction

Purpose of the Paper

The primary aims of this paper are to review and synthesize the literature on the associations of ventilation rates in commercial buildings with health and other human responses, to provide a better scientific basis for setting health-related ventilation standards. We were particularly interested in the following human responses due to their widespread occurrence and potentially great economic impact (Fisk and Rosenfeld, 1997, 1998): (1) communicable respiratory illnesses; (2) sick building syndrome symptoms; and (3) unacceptability or poor quality of air as perceived by occupants or sensory panels. The secondary aims are to point out strengths and weaknesses of study methodologies and to suggest energy efficient approaches for achieving the benefits of increased ventilation.

Sick Building Syndrome Symptoms

During the last 20 years, numerous studies both in Europe and North America have indicated that non-specific symptoms related to occupancy in office buildings are common among the office workers, and that there is considerable variation in the prevalence of symptoms among buildings. These symptoms are generally referred to as sick building syndrome symptoms. According to a World Health Organization working group (WHO, 1983) the sick building syndrome (SBS) is characterized by the following: eye, nose and throat irritation; a sensation of dry mucous membranes and skin; erythema (skin redness); mental fatigue; headache; a high frequency of airway infections and cough; hoarseness; wheezing, itching and non-specific hypersensitivity; nausea and dizziness. SBS is often also characterized by other non-specific symptoms such as: nasal dryness; nasal congestion (stuffy, blocked nose); nasal excretion (runny nose); pharyngeal symptoms; difficulty in concentration; and difficulty in breathing and tight chest. SBS symptoms are associated with occupancy in buildings and dissipate or decrease when

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the individual is absent from the building. The term "SBS" is used primarily when the agents causing the symptoms are unidentified and the symptoms do not indicate a specific known disease.

Ventilation Rates and their Relationship to Indoor Air Quality (IAQ)

In this paper, the term ventilation refers to the flow of outdoor air to a space, either through the ventilation system or by infiltration through the building envelope; this is always accompanied by an equal flow of indoor air to outdoors. Ventilation brings outdoor air to the occupied zone and removes or dilutes indoor-generated pollutants. Ventilation air can be supplied to rooms through mechanical ventilation systems or with the help of natural forces such as wind pressure and the buoyancy effects caused by air temperature differences between indoor and outdoor air. Ventilation air supplied to the spaces can be mixed with recirculated return air or be entirely outdoor air.

Ventilation does not directly affect occupant health or perception outcomes, but the rate of ventilation affects indoor environmental conditions including air pollutant concentrations that, in turn, may modify the occupants' health or perceptions. The air pollutant concentrations in a given space depend on several factors other than ventilation air flow rate. In principle, steady state concentrations in a well-mixed indoor space can be calculated from the following simple equation:

$$C_{in} = C_s + [(S/V)/(\lambda_v + \Sigma\lambda_{other})] \quad (1)$$

where C_{in} = the indoor concentration, C_s = the concentration in the air entering the space, S/V = the indoor pollutant generation rate per unit air volume, λ_v = the air exchange rate equal to the outside air flow rate divided by the indoor volume, and $\Sigma\lambda_{other}$ = the sum of all other indoor pollutant removal rates.

In practice, the situation is not as simple as suggested by the equation. Equation 1 assumes a uniform pollutant concentration in the space. Mixing, however, is not necessarily complete, and the concentration of pollutants at the breathing zone may vary significantly depending on the air distribution pattern and the locations of pollutant sources. The indoor pollutant generation rate (source strength) is usually not constant. Pollutants may be adsorbed by room surfaces during high concentration periods and desorbed again into the air during low concentration periods. Indoor pollutant source strengths are highly variable among buildings, and considered the biggest cause of the variation in pollutant concentrations among buildings (Turk et al., 1987). In many buildings, ventilation rates are not constant. For example, ventilation systems may not operate at night, and rates of ventilation during operation may change with internal heat loads or with outdoor air temperature. Pollutant concentrations may not reach equilibrium until several hours (if ever) after ventilation rates stabilize. Thus, the indoor air quality is also dependent on the operating schedule of the ventilation system. Additionally, the concentration of pollutants in the air entering the space is affected by five major factors: (1) the level and type of pollutants outdoors; (2) possible recirculation of return air; (3) the location of the outdoor air intake relative to outdoor air pollution sources including exhaust air outlets; (4) pollution sources in the air handling system; and (5) pollutant removal from supply air by filters, sorbents, or deposition on duct surfaces. Thus, with a given ventilation rate, indoor air quality may vary significantly due to variations in the quality of the supply air (Björkroth et al., 1998; Seppänen, 1999).

The brief summary above illustrates that ventilation rate, though important, is one of many factors affecting indoor air quality. The association of ventilation rates with health outcomes and perceived air quality will vary among buildings and also within individual buildings over time. Consequently, the average or typical relationship between ventilation rate and health from studies of large numbers of buildings is not likely to apply precisely to specific individual buildings. Additionally, the complex relationship between ventilation rate and indoor air quality makes it difficult to draw conclusions about the effects of ventilation rates from studies in which the confounding influences of other important factors are not controlled in the study design or during the data analyses.

Indoor Carbon Dioxide

Many investigations of the association of indoor carbon dioxide concentrations with health and perceived air quality (PAQ) have been reported. At the concentration range encountered in normal indoor environments (350–2,500 ppm), CO_2 is not thought to be a direct cause of health effects (ACGIH, 1991). However, because occupants are the dominant indoor source of CO_2, the increase in indoor CO_2 concentration above the outdoor concentration (approximately 350 ppm) is considered a good surrogate for the indoor concentrations of bioeffluents (e.g., body odors). Additionally, other indoor pollutants may be generated and vary in rough proportion to occupant-generated CO_2; for example, emissions from office equipment.

The indoor CO_2 concentration is also often considered to be a surrogate for the rate of ventilation per occupant. However, the indoor CO_2 concentration will vary with time even if the ventilation rate and occu-

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pancy are constant and, as discussed later, the CO_2 concentration is often a poor indicator of ventilation rate.

Ventilation and Energy Use

Ventilation consumes energy, primarily because the ventilation air is thermally conditioned, i.e., heated, cooled, and dehumidified or humidified. In mechanically ventilated buildings, the operation of ventilation fans also consumes energy. The capacity of heating and cooling equipment must also be increased as the amount of ventilation air provided increases. Thus, ventilation rates have often been minimized, particularly after the energy crisis in the early 1970s, in order to reduce equipment and energy costs. Buildings, particularly those in cold climates, have also become more airtight which has reduced ventilation air flow through the building envelope. The ventilation rates selected for buildings must strike a balance between energy consumption by ventilation and the known or postulated benefits of ventilation to health and comfort.

Orme (1998) has performed one of the most comprehensive assessments of energy use for ventilation. In a set of 13 countries participating in the IEA Energy Conservation in Buildings & Community Systems Program, the primary energy[1] consumption attributable to the ventilation of all buildings is estimated to equal 9% of the total primary energy consumption of the countries. An estimated 3 exojoule (EJ) of energy[2] are used annually to ventilate US residential buildings, approximately 30% of the total energy used in these buildings. In the US service sector (e.g., commercial, institutional, and government buildings), the estimated energy consumed for ventilation is ~1.5 EJ, approximately one quarter of total service-sector building energy use (Orme, 1998). The annual carbon dioxide emissions attributed to ventilation are approximately 1,000 and 800 million tons for the US residential and service sectors, respectively. Climate has a large influence on the energy required to thermally condition ventilation air. In Europe, most of this energy is used for heating the ventilation air. In the US, significant energy is used for both heating and cooling. In the humid Miami climate, 86% of the energy is used to remove moisture from the ventilation air.

In American-style commercial building ventilation systems with air recirculation, the ventilation rate often has a negligible influence on the energy consumption of fans in the ventilation system; however, energy is required to thermally condition the ventilation air. In European-style ventilation systems without air recirculation, both fan energy and energy for thermal conditioning are affected by the ventilation rate, but the common use of heat recovery from the ventilation air decreases the influence of ventilation rate on building energy consumption.

Ventilation Rate Measurements

The total ventilation rate, because it includes infiltration through the building envelope as well as outdoor air flow through the ventilation system, can usually be measured only by tracer gas methods. In buildings without air recirculation, the ventilation rate can also be determined with reasonable accuracy by measuring supply or exhaust air flow rates. The choice between supply and exhaust flow rate measurements should be based on the indoor air pressure relative to that outdoors. Typically, to reduce moisture problems, the design intent is to underpressurize buildings in cold climates and to overpressurize buildings in warm climates. In underpressurized buildings, the measurement of exhaust flow gives a good estimate for the total ventilation rate, and in over-pressurized buildings the measurement of supply flow rate indicates the total ventilation rate. If return air is mixed with outdoor air and recirculated back to the rooms, the supply flow rate must be multiplied by the proportion of outdoor air in the supply air stream which is measured by a tracer gas procedure or estimated from CO_2 measurements in the return air, outdoor air, and mixed air.

Ventilation rates are also inferred from carbon dioxide measurements. Occupants generate carbon dioxide, causing indoor carbon dioxide concentrations to exceed outdoor concentrations. According to Equation 1 the ventilation rate can be estimated if the carbon dioxide source strength and the concentrations of supply air and room air are known (ventilation is the only significant process for carbon dioxide removal). Indoor and outdoor CO_2 concentrations are measured and the indoor CO_2 source strength is based on the number of occupants in a building and an estimate of their CO_2 production. However, this method is subject to several sources of error which are described in detail elsewhere (Persily, 1997; Mudarri, 1997) (ASTM D 6245-98) and summarized below:

- Carbon dioxide concentrations have often not stabilized when the measurements are performed, and the use of non-steady-state values of carbon dioxide concentration in a steady-state mass balance equa-

[1] Primary energy use is higher than the energy consumed within the buildings because of the losses during energy production and transmission to the building.

[2] Energy consumed in the building, which is less than primary energy consumption.

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tion usually leads to overestimation of the ventilation rate.

- Carbon dioxide concentrations are often measured using instruments, such as indicator tubes, with large potential errors.
- Concentrations of carbon dioxide in outdoor air vary with location and time, and significant error may result if assumed outdoor concentrations are used in calculations.
- The number, weight, activity and diet of the occupants affect the indoor carbon dioxide generation rate and each of these parameters can only be estimated.
- Indoor carbon dioxide concentrations may be spatially non-uniform and measurements at a few locations may not accurately represent the average concentration in the exhaust air.
- Use of the peak CO_2 instead of actual steady state values may produce erroneous ventilation rate estimates, off by a factor of 2 at low ventilation rates, and less at higher ventilation rates (Persily and Dols, 1990).

Measurement of Carbon Dioxide Concentration

Measurement methods for carbon dioxide are described elsewhere (e.g., IPMVP IEQ-Committee, 1999). The sampling strategy for CO_2 is extremely important. The indoor CO_2 concentration will generally be spatially non-uniform and measurement protocols should be designed to determine the average CO_2 concentration in the breathing zone or in the exhaust air streams. Precautions are necessary to avoid measurements in air directly exhaled by building occupants. The CO_2 concentration is seldom at steady state in real buildings because of variations in occupancy and ventilation rates. If occupancy and ventilation rate are reasonably stable, the time required to reach steady state depends on the ventilation time constant which is the reciprocal of the air exchange rate of the space; e.g., if the air exchange rate is 0.5 h^{-1} the time constant is 2 h. A period of three time constants with a stable occupancy and ventilation rate is required for CO_2 concentrations to reach 95% of their steady state value. Three time constants corresponds to 6 h if the air exchange rate is 0.5 h^{-1} and to 3 h if the air exchange rate is 1 h^{-1}.

Ventilation Codes and Standards and Carbon Dioxide Guidelines

The minimum allowed or recommended rate of ventilation is described in national and international building codes and standards. Most commonly, ventilation is expressed in the codes as volume flow of outdoor air, either per occupant or per floor area. In some cases, particularly in residential applications, the ventilation rates may be expressed as minimum air change rate (flow rate per unit indoor air volume) or as a minimum flow per room. Uncertainty regarding appropriate minimum ventilation rates is apparent from the variation among current guideline values and the variation among standards during recent decades. Since 1981, the guideline values have varied from 2.5 Ls^{-1} per person (ASHRAE, 1981) to 20 Ls^{-1} per person (NKB 61, 1991). Currently for non-residential buildings, the guideline values in major standards are close to 10 Ls^{-1} per person. This number is derived from laboratory experiments in which a visiting panel of judges has evaluated the acceptability of the odor in a room containing only sedentary occupants as the pollution sources (Cain et al., 1983; Fanger and Berg-Munch, 1986). Approximately 20% of the panel is dissatisfied when the ventilation rate is 7–8 Ls^{-1} per person. Dissatisfaction among no more than 20% is the criterion for acceptable of indoor air quality in some standards (ASHRAE, 1989). However, in real buildings occupants are not the only pollution source, and even though ventilation rates are high enough to dilute the body odors to acceptable levels, a higher percentage of occupants often perceive air quality as unacceptable because of other indoor pollution sources (Bluyssen et al., 1995a, 1995b, 1996).

In addition to minimum ventilation rate standards, some guidelines and standards list a maximum acceptable indoor carbon dioxide concentration, typically 800 ppm or 1,000 ppm. These two concentrations correspond to outdoor ventilation rates of 11.6 and 8.0 Ls^{-1} per person with sedentary activity (ASTM D 6245-98) at steady state when the concentration of carbon dioxide in outdoor air is 350 ppm. A proposed revision of the American ventilation standard (ASHRAE, 1989) and prenormative work for the European ventilation standard (CEN, 1998) have proposed that ventilation rates should be based on loads from both occupancy and buildings.

Methods of Studies Reviewed

Two primary types of field studies have been used to investigate the association of ventilation rates with health and perception outcomes. In cross-sectional studies, a type of observational study, data on health (or perception) outcomes, ventilation rates, and other relevant factors are collected in multiple buildings or building spaces and analyzed with statistical models to determine the strength and uncertainty in the associations of ventilation rates with the health outcomes. A major weakness of this study design is that many fac-

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tors other than ventilation rate which vary among the buildings may influence the health outcomes, confounding the association of ventilation rate with the health outcome. Confounding occurs when a factor related to the outcome is distributed differently in the groups being compared and distorts the relationship being studied. Another potential weakness is that occupants with substantial adverse health effects from an exposure may preferentially leave the buildings or be absent more often. The better cross-sectional studies control for potential confounding factors in the study design or data analyses. Cross-sectional studies can find statistical associations but, without other supporting findings, such studies can not confirm cause and effect relationships.

The second major type of study is an experimental or intervention study. In one or more buildings or spaces, the ventilation rate is set sequentially at two or more values and the health outcomes are measured at each ventilation rate. Typically, a few days or a week elapses between the change in ventilation rate and the health assessment. Much of the potential confounding is eliminated with this type of study; for example, personal, job, and most building characteristics are unchanged when ventilation rates are modified. However, there is still a possibility of residual confounding by some parameters, such as indoor temperature, outdoor conditions (temperature, pollen, daylight hours) or job stress, which may vary among the experimental periods, as well as bias from various effects of being studied: placebo effects or repeated questionnaire effects, (Menzies, 1993a; Jaakkola, 1995). Most confounding and bias effects, however, may be in either direction. The stronger experimental studies measure potential confounding factors and control for them in analyses and also simultaneously study a similar control group which is expected to have comparable levels of confounding factors, but experiences no change in ventilation rate. The changes in health outcomes in the control group are used to "correct" the measured changes in the experimental group. Repeating the experiment several times in a single group reduces the limitations of a study without a control group. This single-group experimental design, called an "interrupted time series with multiple replications" is discussed by Cook and Campbell (1979). Regardless of the study design, study participants should not be aware of the experimental conditions – i.e., the study must be blinded, particularly when the outcomes measured are subjective (e.g., questionnaire responses, which are strongly influenced by expectations). Ideally, researchers who interact with participants should also be blinded.

The previous paragraphs have referred to potential confounding of the observed associations of health outcomes with ventilation rates. Table 1 lists some of the factors that are potential confounders because they vary among buildings or with time and have commonly been associated with SBS symptoms (Mendell, 1993a, 1993b; Menzies and Bourbeau, 1997). Unfortunately, some studies have controlled for few or no confounding factors, either in statistical analyses or through use of appropriate control groups.

Objectives

Our primary aim was to review the evidence for the association of ventilation rate or CO_2 concentration with health and other human responses in commercial and institutional buildings, based on the studies done to date. We wanted to answer the following more specific questions:

1. Does the magnitude of ventilation rate or carbon dioxide concentration, within the normally encountered range, affect human health and other human responses?
2. Can a "no-effect" threshold value for the ventilation rate (or carbon dioxide concentration) be found, above (or below) which the prevalence of negative outcomes does not change measurably?
3. Can an average dose-response relationship between ventilation rates or carbon dioxide concentrations and human responses be inferred from existing research data?

Table 1 Examples of potential confounding factors in studies of ventilation rates and SBS symptoms

Personal Characteristics	Work-Related Factors	Building-Related Factors	Indoor Environmental Factors
Gender	Job stress or satisfaction	Type of ventilation system	Air temperature
Atopy (allergic disposition)	Use of carbonless copy paper	Type of humidification	Air humidity
History of asthma	Use of or proximity to photocopy machines	Quantity of carpet or textile surfaces	Environmental tobacco smoke
Smoking history	Use of video display terminals	Sealed windows	Dusty surfaces
Job type		Building age	
Medical treatment (especially for asthma and atopy)			

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Approach

General approach

Our general approach was to identify the relevant papers for the study, to set criteria for including studies in the review, to analyze the available information from studies included, to process the results into a common format, and finally to draw conclusions. The papers were identified through literature searches from the following databases: Medline; Current Contents; Byggdok (a database supported by the Swedish Council for Building Research); Airbase (a database maintained by the Air Infiltration and Ventilation Centre of the International Energy Agency); and a database of the papers published by the American Society of Heating Refrigerating and Air Conditioning Engineers (ASHRAE). In order to include studies presented at conferences, we also identified relevant papers from proceedings of the following conference series: International Conferences on Indoor Air Quality and Climate, International Conferences on Healthy Buildings, and Indoor Air Quality Conferences organized by ASHRAE. In addition we used our personal contacts to collect research publications relevant to the topic.

Study Inclusion Criteria

The power and precision of a cross-sectional study increases with the number of study buildings or study spaces in which ventilation rates or CO_2 concentrations and occupant health outcomes are measured, and also with the number of participants. Increased power reduces the effects of random error, but does not reduce systematic bias. We excluded from consideration any cross-sectional studies with only two buildings or study spaces. We excluded cross-sectional studies not including statistical analyses. We considered potential confounding so important in cross sectional studies that we excluded any studies where confounding by personal factors was not controlled either through statistical means, by including approximately similar comparison spaces, or through restrictions in the study population. We included studies which assessed indoor air quality with a human panel, because use of the same panel as an instrument across study spaces and common training of panel members reduces variation in assessments due to personal differences.

In summary, the criteria for including cross-sectional studies in the review were: (1) at least three buildings or ventilation zones; (2) statistical analysis of results; and (3) control for confounding by personal factors as described above.

Among experimental studies, we excluded from consideration: experiments with changes in the type of air handling system or with movement of occupants to a different building; studies that did not either use a control group or repeat the experiment, (e.g., change between baseline and modified ventilation rates) more than once in the same group; studies in which the subjects were obviously or most likely aware of the timing of the changes in ventilation rates; and studies that did not use statistical analyses to evaluate the data (unless a substantial change in symptoms was obvious from a plot of the data).

All studies which fulfilled the criteria described above were included in our review whether or not statistically significant associations were reported. We were forced to reject almost half of the studies dealing with the topic due to one or several exclusion criteria.

As a further criterion of quality among the included studies, we noted those published as peer reviewed articles.

Processing of the Study Data

In our review we used the information reported in the papers; however, some of the desired study information was not provided unambiguously. In some cases authors were contacted, but the information requested was not provided in all cases. Lacking such guidance, it was necessary to use our judgement to make interpretations, which may have led to some errors. If ventilation rates were not provided in the desired form, they were calculated from information available, sometimes supplemented by default assumptions. As a primary indicator of the magnitude of ventilation we used outdoor air flow rate per person (Ls^{-1} per person). This was the most commonly reported ventilation rate metric in the reviewed studies, and the metric often used in codes and standards. If the total ventilation rate (mechanical supply plus infiltration) was measured and reported we used it to estimate ventilation rate per person. If only the supply or exhaust air flow rates were measured, we estimated ventilation rates from reported flows and occupancies. In the study by Brundage et al. (1988), we assumed 17 Ls^{-1} per person supply air flow rate in old barracks, equal to the reported supply air flow rate in the new barracks. Reported recirculation rates of 95% in new barracks and 60% in old barracks were used to calculate ventilation rates. In the study by Drinka et al. (1996) we assumed the supply flow rate to be 13 Ls^{-1} per person, and used reported recirculation rates to calculate ventilation rates. In the study by Zweers et al. (1990), we calculated ventilation rates from reported air exchange rates, and room volume per occupant.

Carbon dioxide measurements were reported inconsistently in studies. Only a few reports specified exactly where and when the measurements were done.

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Table 2 Studies of measured ventilation rates and health or other human outcomes. Several studies include more than one assessment of ventilation data and outcomes

Number of study*	First author of main paper	Year	Study reported also in these papers, see references below	Building selection criteria	Building type	Sealed (S) or openable (O) windows	Smoking	No. of buildings	Type of study	Season	Outcomes assessed	Type of occupants	No. of subjects	Floor area (m^2) per occupant	Reported range of ventilation, Ls^{-1}, pers	Recirculation by HVAC	Humidification	Hours of operation	Ventilation measurement	Confounders controlled in design or analysis	Remarks
1	Bluyssen	1996	1–5	R	O	S, O	Y/N	56	CS	W	SBS, PAQp,o	M/F	6537	13.2	0–56	Y/N	N/Y	N/A	Tr, FM	P, B, W, E	a
2	Brundage	1988		R	B	S, O	N	Several	CS	WY	ARD	M	2.6×10^6	10	1.2–10	Y	N/A	24	E	P, B	b
3	Cochet	1995		R	O	S, O	N/A	6	CS	W	SBS	M/F	615	14–25	4.2–19.8	Y/N	Y/N	N/A	Tr, FM	P, B, W	c
4	Drinka	1996		NR	NH	N/A	N/A	4	CS	W	Influenza	E	690	N/A	3.9–13	Y/N	N/A	24	E	N/A	d
5	Gamble	1986		C	O	S	Y	1	CS	W	SBS	M/F	1115	N/A	0–60	Y	N/A	N/A	FM	P	e
6	Hoge	1994		C	J	N/A	Y	1	CS	F	Pneumonia	M	6700	3.2–7.4	2.0–3.8	Y	N/A	24	FM	P	f
7	Jaakkola	1991a	6	C	O	O	Y	1	CS, Exp	W	SBS	M/F	1719	N/A	0–70	N	N	10	FM	P, W, B	g
8	Jaakkola	1994		NR	O	O	Y	2	Exp	W	SBS, PAQo	M/F	75	N/A	6–23	Y	N	10	Tr, FM	P, W, B	h
9	Jaakkola	1995		R	O	O	N	14	CS	W	SBS	M/F	399	N/A	2.5–>25	N	N	N/A	Tr, FM	P, W, B, E	j
10	Menzies	1993a		N	O	S	Y/N	4	Exp	Sp, F	SBS	M/F	1546	N/A	14–30	Y	Y	N/A	CO_2	P, W, B	k
11	Milton	1999	7	NR	O, M	S	N/A	40	CS	WY	Sick leave	M/F	3720	N/A	12.0–24.0	Y	Y	N/A	CO_2	P, W	l
12	Nordström	1995a	8	R	H	O	Y/N	8	CS	W	SBS, PAQo	F	235	N/A	0.6–17.2	N	N	24	FM	P, B, E	m
13	Palonen	1990		NR	O	O	Y/N	5	CS	W	PAQo	M/F	580	N/A	<2.5–>15	Y	N	N/A	FM	P	n
14	Ruotsalainen	1994		R	DC	O	N	30	CS	W	SBS	F	268	N/A	0–11	N	N	N/A	FM	P, W, B	nn
15	Smedje	1996		R	S	O	N	11	CS	Sp	Performance	C	627	N/A	0.1–19	N	N	N/A	FM	P, B, E	o
16	Sundell	1994	9–11	R	O	O	Y/N	160	CS	W	SBS	M/F	4943	6–15	<2–50	Y/N	Y/N	N/A	TR, FM	P, B, W	p
17	Wu	1996		C	O	S	N	2	Exp	N/A	SBS	M/F	46	2.3–3.4	4.2–20.8	Y	N/A	N/A	FM	P, B	r
18	Wyon	1992	12	C	H	O	N	1	Exp	W	SBS	M/F	561	6.6–10.0	12.0–24.0	N	N	24	FM	P, B	s
19	Wålinder	1998	13	R	S	N	N	12	CS	W	Nasal	M/F	279	N/A	1.1–9.0	N	N		Tr	P, B, E	ss
20	Zweers	1990		NR	O	O	N/A	4	CS	W	PAQp (acc)	M/F	53	6.1–9.8	5.9–19.6	N/Y	N	N/A	FM	P	t

Building selection criteria: R=representative, NR=non-representative, C=complaint buildings. Outcomes: SBS=SBS symptoms, PAQ=perceived air quality by occupants (o) or by panel (p), ARD=acute respiratory disease. Building type: O=office building, S=school, NH=nursing home, J=jail, M=light manufacturing, DC=day care center. Type of study: CS=cross sectional, Exp=experimental. Season: W=winter, Sp=spring, S=summer, F=fall, WY=whole year. Type of occupants: F=female, M=male, C=children, E=elderly people. Ventilation measurements: Tr=trager gas, FM=flow measurements, CO_2=estimated from carbon dioxide concentration, E=estimated from HVAC data. Controlled counfounders: P=personal factors, W=work related factors, B=building factors, E=environmental factors. References: 1=Bluyssen et al. (1995a), 2=Groes et al. (1995), 3=Groes (1995), 4=Roulet et al. (1995), 5=Bluyssen et al. (1995b), 6=Jaakola (1991b), 7=Milton et al. (1998), 8=Nordström et al. (1995b), 9=Sundell et al. (1994a), 10=Sundell et al. (1994b), 11=Stenberg et al. (1994), 12=Wyon et al. (1991), 13=Walinder et al. (1997). * Published as a peer-reviewed article if the study number is bold

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a) Includes 7 naturally ventilated buildings and various ventilation systems, 56 buildings in 9 countries, 226 measured rooms include open spaces and private offices
b) Number of subjects: Assumed 10 m^2 per trainee, 2.6×10^6 trainee weeks corresponds 50,000 trainee years, exact number of buildings is not available
c) Buildings were also part of the European Audit Project, Study #1, includes a few naturally ventilated buildings
d) Ventilation calculated from 30 and 70% recirculation rates assuming supply air flow rate of 13 Ls^{-1} per person
e) Only office floors 2–7 included in the comparison, mold damage was suspected, study included a control building
f) Overcrowded jail, with high occupant density
g) Mechanical supply to hallways, exhaust from offices, ventilation rates changed in some parts of the building, one part as reference
h) No significant pollution sources in buildings, 70/ and 0% recirculation rates, supply air flow was constant, double-blind six week cross-over experiment
i) Subset of 14 buildings from original random sample of 41 buildings with similar air-handling system
j) Two-week blind cross-over experiment
k) Original sample of 65 buildings included office, trade and manufacturing workers in 150 floors, ventilation estimated from CO_2 measurements and design
l) 8 geriatric hospitals, rotary heat recovery systems, ventilation range is the range of means, number of rooms not available, only workers included in the study
m) 5 buildings with various ventilation systems
n) Windows closed during the measurements, but used for airing during the operation hours
o) 11 schools with various ventilation systems, 4 natural ventilation systems included, subjective impaired mental performance of pupils as outcome
p) Heterogeneous buildings with respect to ventilation characteristics and other building factors, sample includes also small (<15 occ) buildings, and a few naturally ventilated buildings
q) Experiments in two office buildings, with high occupant density
r) Hospital building, ventilation experiment limited to two sections of building
s) Included 4 buildings with natural ventilation
t) Buildings are subset from Danish Town Hall study

Some studies used average values, some peak values, and some representative afternoon values. Some assessments used the building average in the analysis, while some used work station concentrations. A number of studies estimated CO_2 concentrations with detection tubes, which is a less precise method than the use of infrared or other type of analyzers.

Estimation of Relative Risks from Prevalence Odds Ratios

Studies have generally reported the strength of associations as relative risks or odds ratios, often adjusted for confounding factors. The relative risk (RR) is generally the prevalence of the outcome in the group with higher prevalence divided by the prevalence of the outcome in the group with lower prevalence (sometimes the reciprocal is reported). The odds ratio (OR) is defined by the equation

$$OR = [a/(1-a)]/[b/(1-b)] = RR\ (1\text{-}b)/(1-a) \quad (2)$$

where a and b in cross-sectional studies are prevalences of the outcomes in the two groups. If odds ratios were reported in the study, the relative risk (i.e., a/b) has been estimated from Equation 2, using reported symptom prevalences. When a and b are less than ~0.2, the OR and relative risk are quite similar numerically. An OR or RR equal to 1.0 denotes no increased risk.

Results

Description of Ventilation Studies

Table 2 summarizes the major features of the studies with measured ventilation rates and lists the papers and reports in which the results of the study have been reported. A study may have assessed the association of ventilation rates with multiple health or perception outcomes or performed multiple analyses using different categories of ventilation rates or different subsets of study data. Consequently, many studies provided multiple assessments (see Table 4) of the associations of ventilation rates with human outcomes. The review included almost 30,000 subjects and more than 350 buildings in fifteen cross-sectional and five experimental studies. Fourteen studies were reported in at least one peer-reviewed article. Most studies included male and female office workers, but some studies were performed with special groups: army trainees (Brundage et al., 1988); elderly people in a nursing home (Drinka et al., 1996); inmates in a jail (Hoge et al., 1994); pupils in a school (Smedje et al., 1996); and hospital personnel (Wyon, 1992; Nordström et al., 1995a, b).

The human outcome in most studies was the preva-

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Table 3 Summary of the studies with measured carbon dioxide concentrations and health outcomes or perceived air quality

	Study[$]	Year	Building selection criteria	Building type	Sealed (S) or openable (O) windows	Smoking	No. of buildings	Type of study	Season	Type of occupants	Outcomes assessed	No. of subjects	Outdoor CO_2	CO_2 measurement method	CO_2 sampling strategy	Measured CO_2 range	Recirculation	Humidification	Hours of operation	Controlled confounders	Remarks
1	Aizlewood	1996	NR	O	S, O	N/A	8	CS	W	M/F	SBS, PAQp	1237	N/A	IR, Ac	Cont.+point samples	1528–1781	N/A	N/A	N/A	P, W, B	a
2	Apte	1999	R	O	S, O	N	41	CS	WY	M/F	SBS	1970	N/A	IR	Every 5 min	390–725 (ave)	Y	Y/N	N/A	P, B	e
3	Bluysen*[$]	1996	R	O	S, O	Y/N	56	CS	W	M/F	PAQp, PAQo	5164	N/A	IR, Ac	Cont.+point samples	oa+(4–1500)	Y/N	Y/N	N/A	P, W, B	b
4	Bright	1992	C	O	N/A	Y/N	46	CS	WY	M/F	SBS	Thousands	325	N/A	N/A	350–1750	N/A	N/A	N/A	P	c
5	Carpenter	1990	NR	N/A	N/A	N/A	>8	CS	N/A	N/A	SBS (fatigue)	N/A	N/A	N/A	N/A	500–1750	N/A	N/A	N/A	N/A	
6	Fisk	1993	NR	O	S/O	N	12	CS	S	M/F	SBS	880	330–359	IR	45 h bag sample	370–580	Y/N	N/A	N/A	P, B, W	f
7	Hedge	1995	NR	O	S	N	5	CS	Sp	M/F	SBS	939	N/A	IR	Hourly samples, 3 h	468–664	Y	N/A	N/A	P, W, B	g
8	Hill	1992	NR	O	N/A	N/A	6	CS	W	M/F	SBS	206	325	IR	80 per zone per day	400–850	N/A	N/A	N/A	P	
9	Hodgson	1989	C	O	S	N/A	1	CS		M/F	SBS	105	N/A	DT	Work station, afternoon	300–1250	N/A	N/A	N/A	P, W, B	
10	Hoge*	1994	C	J	N/A	Y	1	CS	F	M	ARD (pneum)	6700	N/A	DT	N/A	1100–2500	Y	N/A	24	P	
11	Janssen	1986	NR	S, O	N/A	N	2	Exp	W	C, M/F	PAQo	222+143	N/A	IR	Return air, continuous	850–1500	Y	N/A	N/A	P, W, B	h
12	Marmot	1997	R	O	S/O	Y	29	CS	WY	M/F	SBS	3332	N/A	N/A	N/A	550–800	N/A	N/A	N/A	P	r
14	Menzies*	1993a	NR	O	S	Y/N	4	Exp	Sp, F	F/M	SBS	1546	N/A	IR	Afternoon	551–901	Y	Y	N/A	P, W, B	
15	Myhrvold	1996	NR	S	O	N	5	CS	N/A	S	SBS, perform	550	N/A	IR	N/A	601–3727	N	N/A	N/A	P	
16	Nelson	1995	NR	O	S/O	N	4	CS	Sp	F/M	SBS	646	N/A	IR	EPA strat.	541–792	N/A	N/A	N/A	P, W, B	
17	NIOSH	1991	C	O	S	N	1	CS	W	F/M	SBS	2145	N/A	IR	4×per day	331–594	Y	N/A	N/A	P, W B	
19	Norbäck	1995	NR	S	O	N	6	CS	SP, F	F/M	PAQo	97	N/A	DT	End of lessons	670–2700	N	N/A	N/A	RR	r
20	Sieber	1998	C	O	N/A	N/A	80	CS	WY	F	SBS	N/A	275–549	IR	Afternoons	370–2463	N/A	N/A	N/A	P	
21	Smedje	1997	NR	S	O	N	38	CS	W	F/M	SBS	1410	375–525	IR	2× after lessons	425–2800	N/A	N/A	N/A	N/A	r
22	Sohn	1994	NR	O	N/A	Y?	5	CS	S/W	N/A	SBS	250	N/A	N/A	N/A	543–951	N/A	N/A	N/A	P, B, W	
23	Zweers	1992	R	O	S/O	Y/N	60	CS	W	F/M	SBS	7043	N/A	N/A	4×, 5 loc per bldng	485–1329	Y/N	Y/N	N/A	P, B	r

*Also in ventilation studies, [$]also reported by Bluyssen et al. (1995a, 1995b); Groes (1995), Groes et al. (1995). [$] Published as peer-reviewed article if study number is bold
Study type: CS=cross-sectional, Exp=experimental. Measurement method: IR=infrared, Ac=acoustic, DT=detection tube. Outcomes: as defined in Table 2

a) British subset of European Audit Project, includes 4 buildings with natural ventilation
b) European Audit Project, 56 buildings in nine countries
c) Office buildings of the US Air Force
e 41 buildings from EPA's base study in 1994–1996
f) Three buildings with natural ventilation included
g) CO_2 concentrations are mean of measurements
h) Ventilation rates controlled by return air CO_2 concentration
r) Sample included buildings with natural ventilation

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lence of SBS symptoms assessed with a self-administered questionnaire. Some studies analyzed results by symptom groups or employed an integrated symptom summation score. The recall period varied considerably between studies (e.g., symptoms last week, symptoms last month, symptoms last year). To reduce errors in the recall of prior symptoms, some studies used questionnaires that asked about current symptom intensity (Wyon, 1992; Jaakkola et al., 1994; Menzies et al., 1993a; Bluyssen et al., 1996). Occupants evaluated air quality in five studies, while trained sensory panels made the evaluations in two studies. Panel members evaluated perceived air quality (PAQ) directly after breathing clean outside air, but occupants were adapted to indoor conditions. In three studies, the health outcome was communicable respiratory illness. In one study, short-term sick leave was the outcome (Milton et al., 1999) and respiratory illness was discussed as a probable contributor to short-term sick leave. One study used a self-rating of impaired mental performance as an outcome (Smedje et al., 1996), while another used nasal patency[3] and biomarkers in nasal lavage (Wålinder et al., 1997, 1998).

A factor which may affect study outcomes is the design and use of windows. In most American studies windows were sealed, while in most of the European studies the windows were openable, although possibly not opened during the study. Most of the studies were performed during the winter when windows are most often closed.

Exposure to environmental tobacco smoke is a potential confounding factor that was not always controlled. In Table 2, a building was considered a nonsmoking building if smoking was restricted to designated areas. Many studies did not report if smoking was allowed or restricted.

The type of air-handling system varied and was not always reported. Some air-handling systems recirculated air and some did not. Some studies included both recirculating and non-recirculating systems. Humidification may also be a confounding factor. Usually, the type of humidification was not specified.

The expected accuracy of ventilation rate measurements varies considerably. Ventilation rate was measured with tracer gases in six studies, and with air flow rate measurements in 10 studies. Carbon dioxide concentrations were used in two studies to estimate the ventilation rates. To calculate ventilation rates from reported recirculation rates, we assumed supply air flow rates (see the Table 2 remarks) in the study by Drinka et al. (1996) and for some of the buildings in the study by Brundage et al. (1988). The reported range in ventilation rate was large, ranging from zero to 70 Ls^{-1} per person. Ventilation rates were reported as zero, when the mechanically supplied air flow rates to a room were zero or too small to measure. These air flow rate measurements do not account for ventilation via air infiltration and inter-room airflows. Ventilation rates of zero are obviously not possible as the long-term average.

The control for confounding factors varied considerably. All SBS studies controlled for some personal factors, 13 studies controlled for work- or building-related factors, and just two cross-sectional studies (Bluyssen et al., 1996; Jaakkola and Miettinen, 1995) attempted to control for environmental factors.

Description of CO_2 Studies

Table 3 summarizes the major features of studies with measured carbon dioxide concentrations. Of the 21 studies, ten were reported in peer-reviewed articles, and all are cross-sectional except for two experiments. Sixteen studies included ventilation in office buildings, four in school buildings, one in a jail, and one in military buildings, presumably offices. The reviewed studies include more than 30,000 subjects in over 400 buildings, of which over 100 were complaint buildings. Three studies reported ventilation rates, and were also included in Table 2.

The most common human outcome was the prevalence of SBS symptoms, assessed with self-administered questionnaires. In four studies, air quality was evaluated by trained sensory panels or by occupants. In one study, the health outcome was communicable respiratory illness (Hoge et al., 1994). One study used a computerized test of mental performance as the outcome (Myhrvold et al., 1996).

As with the ventilation rate studies, most of the CO_2 studies were performed in winter, many failed to control for all suspected confounders, and many failed to report the type of HVAC system and to fully characterize the study buildings.

Association of Ventilation Rates with Health and Other Outcomes

For each study, Table 4 provides the following information (when available): key features of the study; the proportion of statistical tests that identified statistically-significant associations between outcomes and ventilation rates; the range of relative risks; and the range of outcome prevalences. A study may have included one or several assessments of the association of ventilation rate with health outcomes. The different assessments of a single study may, for example, have been performed using different ventilation rates, dif-

[3] An indicator of lack of nasal congestion.

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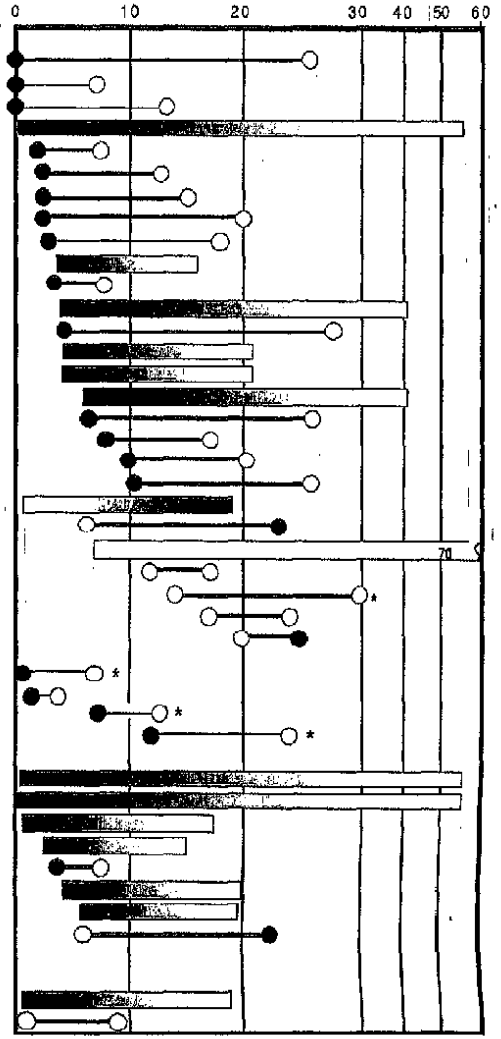
Table 4 Summary of studies with measured ventilation rates per person, and human responses. The circles in the chart denote mean ventilation rates compared in the assessment. A black circle denotes a significantly higher prevalence of the measured outcome. The bars denote findings of dose response relationships between outcome in the indicated range. The darker end of the bar denotes a significantly higher prevalence of measured outcome. A thicker connecting line between data points denotes an experimental study

Study[a]	First author of the paper	Year	Building type	Outcome in the assessment	Recall or (record) period	Associated with ventilation	Number of statistical tests from total showing association with ventilation	No. of bldgs or zones	Zones with measured ventilation	No. of respondents in assessment	Relative risk or (odds ratio)	Prevalence of outcome at reference ventilation rate, %	Remarks
Assessments with sick building syndrome outcome													
7	Jakkola	1991a	O	6 groups of s	1 week	Score (0–6)	1/2	4	Several	676	1.1	N/A	g, h, f
5	Gamble	1986	O	HP+5 s	Now	4 out of 6	2/3	3	3	306	1.8	11–31	f
5	Gamble	1986	O	HP+5 s	Now	5 out of 6	2/3	3	3	338	2.4	8–25	f
1	Groes	1995	O	12 s	Now, 1 mo	Score	Model	56	226	5164	N/A	7–32	d
7	Jaakkola	1991b	O	6 groups of s	1 week	Score (0–6)	1/2	1	Several	149	1.3	N/A	g
7	Jaakkola	1991b	O	6 groups of s	1 week	Score (0–6)	1/2	1	Several	80	1.2	N/A	g
7	Jaakkola	1991b	O	6 groups of s	1 week	Score (0–6)	1/2	1	Several	391	1.1	N/A	g, j
9	Jaakkola	1995	O	13 weekly s	12 mo	7 out of 13	8/14	14	Several	176	5.4–37	0.9–4.3	g, m
3	Cochet	1995	O	12 s	Now, 1 mo	Score	7/11	6	30	615	1.7–3.8	N/A	e
16	Sundell	1994	O	3 groups of 12 s	3 mo	Score	Model	160	600	3926	(2–3)	N/A	p
14	Ruotsalainen	1994	DC	9 s	12 mo	1 out of 9	1/13	30	30	268	2.8	23.2	oo
16	Sundell	1994a	O	3 groups of 12 s	3 mo	General s	2/3	27	>54	725	N/A	20	q
16	Stenberg	1994	O	3 groups of 12 s	4 mo	Score	2/3	N/A	Many	292	(1.87)	N/A	qq
17	Wu	1996	O	4 s	N/A	3 out of 4	4/4	1	25	28	N/A	24–50	s, t
17	Wu	1996	O	4 s	N/A	3 out of 4	4/4	1	25	18	N/A	17–34	ss, t
16	Sundell	1994a	O	3 groups of 12 s	3 mo	General s	2/3	24	>48	625	N/A	10	r
7	Jaakkola	1991a	O	6 groups of s	1 week	Score (0–6)	1/2	4	Several	591	1.1	N/A	g, h
16	Sundell	1994b	O	3 groups of 12 s	3 mo	Score	1/1	N/A	266	266	(1.8)	N/A	
9	Jaakkola	1995	O	13 weekly s	12 mo	4 out of 13	5/14	14	Several	294	5.0–6.0	3.0–5.0	g, m
7	Jaakkola	1991a	O	6 groups of s	1 week	Score (0–6)	1/2	4	Several	609	1.1	N/A	g, h
12	Nordström	1995a	H	13 s	3 mo	2 out of 13	2/13	8	N/A	225	(1.9–2.6)	23–28	yyy
8	Jaakkola	1994	O	4 groups of 13 s	Daily	2 out of 13	2/15	2	72	72	0.35–0.46	N/A	l
7	Jaakkola	1991a	O	6 groups of s	1 week	None	1/2	1	410	938	N/A	N/A	ee
18	Wyon	1992	H	18 s	N/A	None	?	1	2	51	N/A	N/A	u
10	Menzies	1993a	O	7 s	Now	None	0/3	4	200	637	0.8–1.2	15–39	o
18	Wyon	1992	H	18 s	N/A	None	?	1	3	65	N/A	N/A	u
9	Jaakkola	1995	O	13 weekly s	12 mo	3 out of 13	3/14	14	Several	175	4.2–5.2	4.3	g, m, j
Studies with respiratory disease or absence outcome													
2	Brundage	1988	B	ARD	(4 years)	ARD	24/30	Many	N/A	2.6×10^6	1.51	0.46	a
6	Hoge	1994	J	Pneumonia	(4 weeks)	Pneumonia	1/1	1	49	6700	1.94	0.3	
4	Drinka	1996	NH	Influenza	(4 mo)	Influenza	1/1	4	N/A	396	2.2–4.7	3–20	b
11	Milton	1999	O, M	Absence	1 year	Sick leave	1/3	40	110	3364	1.53	1.5	c
Assessments with perceived air quality as outcome													
1	Bluyssen	1995a	O	Decipols	Now	1/1	Model	56	226	5164	N/A	N/A	d, v
1	Groes	1995	O	PAQ	Now	1/1	Model	56	226	5164	N/A	30	d, w
12	Nordström	1995b	H	Stuffy air, odor	3 mo	2/2	2/2	8	N/A	225	(0.3–0.4)	24–44	yy
13	Palonen	1990	O	Odor, dust, stuff	1 week	2/3	2/3	5	Many	580	1.9–2.8	N/A	z
14	Ruotsalainen	1994	DC	Odor, body odor	12 mo	1/2	1/2	30	30	268	2.8	19.5	
3	Cochet	1995	O	Dissatisfaction	Now	1/1	Plot	5	25	522	N/A	5–35	y
20	Zweers	1990	O	PAQ	Now	1/5	1/5	8	8	12	N/A	?	zz
8	Jaakkola	1994	O	Odor, dust, stuff	Daily	1/3	1/3		72	72	0.47	N/A	
Assessments with other outcomes													
15	Smedje	1996	S	SMP	N/A	1/1	1/1	Many	28	627	(0.9)	N/A	x
19	Wålinder	1998	S	Nasal	N/A	5/5	5/5	12	24	279	N/A	N/A	xx



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* These ventilation rate estimates may have higher uncertaintites because they are based on carbon dioxide measurements or rely on assumed supply air flow rates
[5] Published as a peer-reviewed article if study number is bold
Building type: O=office building, S=school, NH=nursing home, J=jail, H=hospital, M=light manufacturing, DC=daycare. Study type: CS=cross-sectional, Exp=experimental. Outcome: PAQ=perceived air quality (o=occupants, p=panel); SBS (sick building) symptoms, SMP=subjective mental performance, HP=hypersensitivity pneumonitis. General remarks: 1) Room height of 3 m has been used to calculate ventilation rates. 2) Buildings are considered non smoking buildings if specific smoking areas have been designated, Y/N in smokin column denotes that the study included smoking and non smoking buildings

a) Assumed 17 L/s per person supply air flow rate barracks, equal to the reported supply air flow rate in the new barracks. Reported recirculation rates of 95% in modern barracks and 60% in old barracks
b) Ventilation rates estimated assuming supply air rate of 13 L/s per person and reported reciculation rates of 30 and 70%, RR=4.7 for cultured-confirmed influenza, and RR=2.2 for other illnesses (statistically not significant), prevalence=3% for influenza and 20% for other illnesses
c) Risk ratio RR=1.53 for short-term sick leave, 2.3 for total sick leaves, prevalence for short-term sick leave excluding those with disability payments
d) 56 buildings in 9 countries, range of prevalences of 12 symptoms experienced now
e) Ventilation rates are means of the buildings with low symptom and high symptom prevalence
ee) Adjusted SBS score lower with higher ventilation rates, but not significantly
f) Mechanical ventilation rate=0 L/s, pers., natural ventilation and infiltration not measured. HP symptoms also associated with ventilation but not statistically significant
g) Denoted ventilation rates are means of reported ranges, number of ventilation measurements is subset of total 410 measurements, symptoms 3 weeks after change in ventilation
h) High ventilation rate is the average for the building, lower ventilation corresponds the reduction of 60, 75 or 100% reduction in ventilation
j) Upper end of ventilation range means higher than indicated value
l) Constant supply air flow, 72 selected sensitive subjects, only one week exposure at each ventilation rate
m) Subset of 14 buildings with similar ventilation system from original sample of 41 buildings, no recirculation, no humidification
n) Dose response indicates the increase of most SBS symptoms in the range of 0 to 25 L/s, person, relative risk for individual symptoms is 1.1–1.3 per L/s, person
o) Ventilation estimated in the study from CO_2 concentrations
oo) Only one of nine symptoms showed the raltionship with ventilation rate
p) Odds ratio 2–3 for SBS score at dichotomous cut-off points within the indicated ventilation range
q) Dose response relationship for the prevalence of general symptoms for women, Sundell (1991) reports also dose-response relationship for mucous membrane and skin symptoms
qq) Reports also OR=1.5 for increase of SBS between 28 and 11 Ls^{-1} per person but not statistically significant
r) Dose response relationship for the prevalence of general symptoms for men, Sundell (1991) reports also dose response relation for skin symptoms
s) Mixing air distribution
ss) Laminar air distribution
t) No statistical analysis in the paper, but plotted results show strong relationship between ventilation rate and chest distress, dizziness, and headache
u) Baseline ventilation rate was calculated assuming hospital personnel spending 10% of time in treatment rooms and 90% time in patient rooms, prevalence of 11 from 16 reported symptoms increased with decreased ventilation but not statistically significant
v) PAQp evaluated by national panels
w) Dose response relationship based on the statistical model
x) Dose response relationship from multiple regression analysis, odds ratio for subjective impaired mental performance OR=0.9 per change of ventilation 1 L/s per pers
xx) Outcome was objective measurement of nasal cavity and inflammation indicators in the nasal lavage, no association was found with ventilation rate per person but statistically significant association between all five outcomes and air change rate
y) One building with natural ventilation excluded, no statistical analysis but plotted data show a strong relationship between outcome and ventilation rates
yy) Odds ratio 0.3–0.4 per 10 Ls^{-1}, pers for stuffy air and unpleasant odor
yyy) Odds ratio 1.9 per 10 Ls^{-1}, pers for facial dermal symptoms and 2.6 per 10 Ls^{-1} per person for eye symptoms
z) Dose response relationship for unpleasant odor and dustiness
zz) Dose response relationship based on significant correlation between acceptability of air perceived by panel of 12 and ventilation rate

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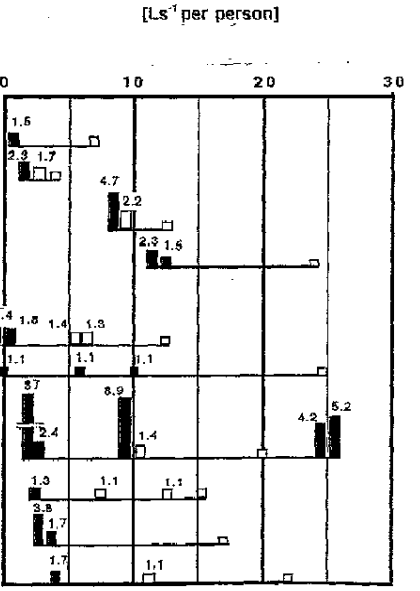
ferent sub populations, or different seasons. Each assessment is described in Table 4 on a single row and noted if reported in a peer-reviewed scientific article. The presence or absence of statistically significant associations of ventilation rates with outcomes is illustrated graphically within the table using an adaptation of the format of Mendell (1993b). For comparison of outcomes at two levels of ventilation rate, each level is represented with a circle, with multiple assessments within single studies displayed separately. Three studies (Bluyssen et al., 1996; Cochet et al., 1995; Ruotsalainen et al., 1994) have both SBS data and perceived air quality as outcomes. These outcomes are presented also separately in Table 4. If the study compared outcomes among groups of workers experiencing different ranges of ventilation rate (e.g., <10 Ls^{-1} per person versus >10 Ls^{-1} per person), the graph presents the approximate mean ventilation rate within each range. Statistically significant differences in outcomes at different ventilation rates are illustrated graphically within the table by shaded circles, shading indicating at least one significantly worsened health or perception outcome at that ventilation rate. If all circles are unshaded for a comparison, this indicates lack of a statistically significant increase in any outcome with ventilation. In general the criteria for statistical significance are $P \leq 0.05$, or a 95% confidence interval that excludes unity.

Several studies have recorded the symptoms experienced at several levels or ranges of ventilation, and analyzed the relationship of ventilation rates with outcomes using statistical models. Some of these analyses indicate a dose-response relationship, i.e., a progressive increase in the risk of the outcome as the ventilation rate decreased. In other instances the ventilation rates were represented as a continuous variable in a model and only a model coefficient or correlation coefficient was provided. If ventilation rate was a significant parameter in the model, the finding was inter-

Table 5 Risk of increased prevalence of respiratory illnesses and sick building symptoms with decreasing ventilation rates in studies with necessary data. The column at the right end of each bar is the reference with a height of one unit. The heights of other columns are proportional to the relative risk at the ventilation rate indicated on the horizontal axis. The dark bars denote statistically significant increases in risk relative risks. Double columns refer to the symptoms with highest and lowest prevalences

Study[§]	First author of paper	Year	Building type	Outcome associated with ventilation rates	Recall or (record) period	Prevalence (%) at reference ventilation rate	Relative risk	Remarks
Studies with respiratory disease outcome								
2	Bundage	1988	B	Actue respir. disease	(4 years)	0.46	1.51	
6	Hoge	1994	J	Pneumonia	(4 weeks)	0.3	1.7–2.3	a
4	Drinka	1996	NH	Influenza, respiratory illness	(4mo)	3	2.2–4.7	b
11	Milton	1999	O, M	Sick leave	(1 year)	1.50	1.5–2.3	c
Studies with sick building syndrome outcome								
5	Gamble	1986	O	5 symptoms	Now	8–25	1.3–2.4	
7	Jaakkola	1991a	O	Score (0–6)	1 week	N/A	1.1	
9	Jaakola*	1995	O	13 symptoms	12 mo	0.9–4.3	1.4–37	
	Jaakkola	1991b	O	Score (0–6)	1 week	N/A	1.1–1.3	
3	Cochet	1995	O	12 symptoms	Now, 1 mo	N/A	1.7–3.8	
16	Stenberg	1994	O	Score	3 mo	N/A	1.1–1.7	



a) Relative risk for three different ventilation rates
b) Relative risk RR=4.7 for influenza, 2.2 for other respiratory illnesses
c) Relative risk RR=1.5 for short-term sick leave, 2.3 for total sick leave, prevalence for short-term sick leave excluding those with disability payments
B, J, NH, O, M: See footnotes of Table 2
* Reference for this study is at 20 Ls^{-1} per person. [§] Published in a peer reviewed article if study number is bold

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preted as a dose-response relationship. These findings of dose-response relationships are presented in Table 4 using a horizontal bar, with the darker shaded end representing a worsened outcome. An unshaded bar indicates that no statistically significant relationship was identified. The ends of the shaded and unshaded bars correspond to the range of ventilation rates in the data analyses.[4] When the ventilation rate has been a continuous parameter in a model, because the model estimates only the average relationship, the maximum ventilation rates for which reported dose-response relationships remain statistically significant usually cannot be determined.

The results in Table 4 have been organized by outcome: sick building syndrome, respiratory disease and absence outcomes, perceived air quality, and other outcomes. Within outcome groups, results were organized by whether a relationship was reported, and within these groups, by the lowest ventilation rate included in the assessment. The results show clearly that the magnitude of ventilation was significantly associated with at least one reported outcome in the majority of the studies. All studies of respiratory illnesses found a significant increase in the risk of illness in the group with a lower ventilation rate. The relative risk for respiratory illness varied between 1.51 and 4.7. Theoretical modeling by Nardell (1997) and Nardell et al. (1991) also predicts that ventilation rates will affect the transmission of respiratory illness. Ventilation rates in studies with respiratory disease outcomes were below typical mean ventilation rates in the other studies.

Of 27 assessments (rows in Table 4) with SBS symptoms as outcomes, 20 found a significantly higher prevalence of one or more symptoms with lower ventilation rates, with relative risks or odds ratios between 1.1 and 6 (with one outlier value of 37). The findings of a significantly increased outcome were particularly consistent when the lower ventilation rate was below 10 Ls^{-1} per person. Only three of 22 such assessments failed to find lower ventilation rates below 10 Ls^{-1} per person to be associated with an increase in at least one symptom or symptom group.

There was no clear ventilation rate threshold above which no further reduction in SBS symptoms occurs. Several studies, particularly those indicating a dose-response relationship (e.g., Sundell, 1994; Jaakkola and Miettinen, 1995) suggested that the risk of sick building symptoms continues to decrease with increasing ventilation rates above 10 Ls^{-1} per person, possibly up to 25 Ls^{-1} per person (Table 5). In the ventilation rate range of 0–25 Ls^{-1} per person, Jaakkola and Miettinen (1995) found odds ratios of 1.01–1.3 for each decrease of 1 Ls^{-1} per person. However, four assessments did not find increases in ventilation rates above 10 Ls^{-1} per person to be associated with a significant change in symptoms.

Three studies found a significant *increase* in the prevalence of symptoms with increases in ventilation rate. Jaakkola and Miettinen (1995) found a significant increase in three out of 13 symptoms (eye, mucosal irritation and allergic reaction) as ventilation rates increased above 25 Ls^{-1} per person. Jaakkola et al. (1994) found a significant increase in two out of 13 symptoms with a lower air recirculation rate, which corresponded to a higher ventilation rate of 23 Ls^{-1} per person. Nordström et al. (1995a) found that two out of 13 symptoms were associated significantly with higher ventilation rates in hospitals.

Worsened air quality as perceived by occupants and panels was associated with lower ventilation rates in 7 out of 8 studies. The results of six studies were interpreted as dose-response relationships. Nordström (1995b) provided odds ratios (3.3 for stuffy air and 2.5 for dustiness) per decrease in ventilation rate of 10 Ls^{-1} per person. These studies also suggest that perceived air quality is improved with increased ventilation rate up to 20 Ls^{-1} per person. The prevalence of perceived inferior air quality is high. In all six studies with a perceived air quality outcome, up to 50% of the occupants have considered the indoor air unacceptable even though the study buildings were considered non-complaint buildings.

By sorting the results, we attempted to determine whether the relationships of ventilation rates with health or perception outcomes were affected by complaint building status, air recirculation, operability of windows, and smoking restrictions. However, the data were inadequate for such assessments. Several studies included buildings with more than one of these characteristics (e.g., some study buildings had operable windows but other study buildings had non operable windows), and not all studies described the buildings in sufficient detail to make exact classification possible. Also restricting the review to the findings of the 14 studies reported in peer-reviewed articles did not substantially affect the interpretation.

Some studies provided the relative risk or odds ratio for the outcome at several different measured ventilation rates, or presented data from which these relative risks could be calculated. A summary of these studies is presented graphically in Table 5. Relative risk

[4] An exception is the shaded bar for the study by Sundell (1994), where the bar is terminated at 17 Ls^{-1} per person because the dose-response relationship is not significant for higher ventilation rates.

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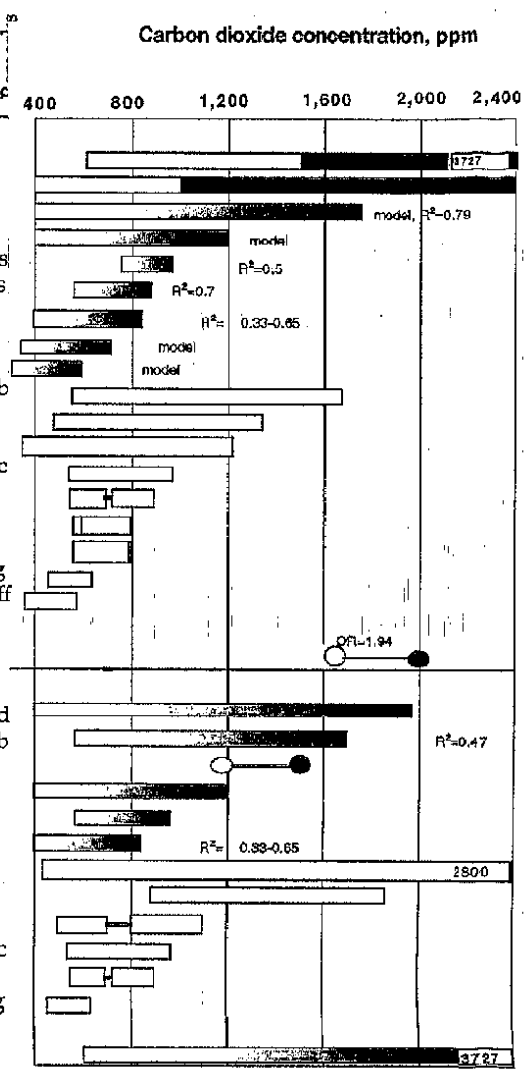
Table 6 Summary of the studies with measured carbon dioxide concentrations and health outcomes or perceived air quality. The bars in the chart denote range or compared concentrations. The dark part of the bar denotes higher prevalence of the measured outcome. Continuously shaded bars denote a dose-response relation in the indicated concentration range. Circles denote mean or median concentrations of compared buildings

Study number*	First author of study	Year	Building type	Outcome in analysis	Recall or (record) period	Outcomes associated with ventilation	Number of zones (z) or buildings (b)	Number of respondents in analysis	Lowest CO_2 concentration in assessment	Highest CO_2 concentration in assessment	Relative risk or (odds ratio)	Prevalence of outcome, %	
Sick building symptoms													
15	Myhrvold	1996	S	Score of 7 s	N/A	Score	22 z	549	601	3727	N/A	N/A	
20	Sieber	1998	O	4 s	N/A	2/4 s		N/A	<1000	>1000	1.85		r
4	Bright	1992	O	12 s	Any	4/12 s	18 b	Thousands	350	1750	N/A	20–90	e
3	Groes	1995	O	12s	Now, 1 mo	s score	56 b	5164	400	1200	N/A	7–32	a
22	Sohn	1994	O	Score of >5 s	N/A	s score	10 z	250	766	951	N/A	N/A	b, s
22	Sohn	1994	O	Score of >5 s	N/A	s score	10 z	250	543	886	N/A	N/A	c, s
8	Hill	1992	O	12 s	Orebro	6/12 s	6 b	206	700	850	N/A	0–34	j
2	Apte	1999	O	21 s	1 mo	6/19 s	41 b	1970	oa+4	oa+360	1.14–1.60		ee
17	NIOSH	1991	O	17 s	Today	2/17 s	30 z	2145	331	594	(8.0)	2–25	o
1	Aizlewood	1996	O	Score of s	Now		8 b	1237	547	1781	N/A	N/A	a, b
23	Zweers	1992	O	12 s	12 mo		61 b	7043	485	1329	N/A	N/A	a
9	Hodgson	1989	O	10 complaints	N/A		1 b	105	300	1250	N/A	N/A	
1	Aizlewood	1996	O	Score of s	Now		8 b	1237	528	956	N/A	N/A	a, c
14	Menzies	1993a	O	7 s	Now		200 z	1546	551–699	727–901	N/A	N/A	m
12	Marmot	1997	O	Score of 10 s	2 weeks		288 z	3332	<500	>500	N/A	7.2–49.8	l
16	Nelson	1995	O	19 symptoms	4 weeks		4 b	646	541	792	N/A	1.3–38.1	
7	Hedge	1996	O	15 symptoms	1 mo		5 b	939	468	664	N/A	2.2–28.2	f, g
6	Fisk	1993	O	6 groups 15 s	1 yr, 1 wk		25 z	880	370	580	N/A	N/A	a, ff
Respiratory diseases													
9	Hoge	1994	J	Pneumonia	(4 weeks)	Pneumonia	1	6700	1654	2000	1.94	0.3	
Perceived air quality													
3	Bluyssen	1996	O	PAQp	Now	Decipols	56 b	9×12 (panel)	oa+4	oa+1500	N/A	N/A	a, d
1	Aizlewood	1996	O	PAQo	Now	Decipols	8 b	12 (panel)	547	1781	N/A	N/A	a, b
10	Janssen	1986	S	PAQo	Now	Stale-fresh	1 b	222	1180	1540	N/A	N/A	k
3	Groes	1995	O	PAQo	Now	Acceptab.	57 b	5164	400	1200	N/A	N/A	a
21	Sohn	1994	O	Discomfort	N/A		11 z		543	970	N/A	N/A	t
7	Hill	1992	O	PIAQo	N/A	Odor, stuffy	6 b	206	<500	>500	N/A	N/A	h
20	Smedje	1997	S	PIAQo			96 z	1303	425	2800	N/A	N/A	
18	Norbäck	1995	S	PIAQo	6 mo		6 b	97	880	1850	N/A	N/A	q
10	Janssen	1986	B/O	PAQo	Now		1 b	143	500–700	800–1100	N/A	N/A	k
1	Aizlewood	1996	O	PAQo	Now	Decipols	8 b	12 (panel)	528	956	N/A	N/A	a, c
13	Menzies	1993a	O	PIAQo	Now		200 z	1546	551–699	727–901	N/A	N/A	n
6	Hedge	1995	O	PIAQo	1 mo		5 b	939	468	664	N/A	N/A	f, g
Other outcomes													
15	Myhrvold	1996	S	Performance	Now		22 z	548	601	3727	N/A	N/A	



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Building type: O=office building, S=school, J=jail, B=bank. Outcomes: defined in Table 2 except PIAQ=perceived indoor climate (includes factors other than IAQ)
a) Sample includes buildings with natural ventilation
b) Winter
bb) Plotted data suggest relationship between PAQp and maximum CO_2 with $R^2=0.47$
c) Summer
d) CO_2 concentration=difference between indoors and outdoors, national panels in nine countries
e) Even better correlation within buildings with recirculation of air
ee) Analysis of EPA's BASE study data, 41 buildings from 1994–1996, OR=1.14–1.60 per 100 ppm of CO_2
f) Average CO_2 concentration of 45-hour work week sample
ff) Range of prevalences for 12 symptoms reported "now"
g) SBS score included 15 symptoms, PIAQ included 7 indoor climate factors not only IAQ prevalence of symptoms 1–3× month, CO_2 concentration is mean of measurements
h) Plotted data suggest correlation of unpleasant odor and stuffy air to max CO_2 concentration with $R^2=0.43$ and 0.60
i) The paper does not report the relationship but, plotted data suggest correlation of six of 12 symptoms with the maximum CO_2 concentration with $R^2=0.33–0.65$
k) CO_2 controlled ventilation system, two-week periods, blinded test
l) Score formed from 10 symptoms, past 14 days
m) Seven symptoms in two groups irritation of nose, throat or cough, and systemic symptoms: headache, fatigue or difficulty in concentration
n) Environmental dissatisfaction score consists of nine parameters, good correlation between symptoms and environmental dissatisfaction score
o) Odds ratio >1 for 16 of 17 symptoms, statistically significant (OR=8.0 per ln (CO_2) for non specific symptoms (headache and fatigue)
q) Subjective indoor air quality score formed by rating of room temperature, air dryness, dustiness of air
r) From three reported symptoms shortness of breath and chest tightness clearly higher (RR=1.85) in group with CO_2>1,000 than in those <1,000
s) Plotted data suggest correlation between CO_2 concentration and SBS in summer and winter, score includes headache, eye irritation, fatigue, and difficult, concentration
t) Plotted data suggest correlation between CO_2 concentration and IAQ discomfort by occupants
* Published as a peer-reviewed article if study number is bold

is indicated by columns at each ventilation rate assessed, with the height of the column proportional to the relative risk, and the RR value shown above each column. The column on the right end of the connecting line for each study is the reference, with relative risk and column height equal to one. Double columns are used to indicate the range of relative risks for multiple outcomes – the higher of the adjoining double columns represents the highest relative risk and the lower represents the lowest relative risk. Table 5 also shows the prevalences of the outcomes at the reference ventilation rate. Thus, the prevalence of some outcomes at lower ventilation rates can be estimated by multiplying the relative risk at that ventilation rate by the prevalence at the reference ventilation rate.

Association of CO_2 Concentration with Health or Perception Outcomes

The results of the analysis of each study of the association of CO_2 with health and perception outcomes are presented in Table 6, using the same format as Table 4. Findings are organized by outcomes, and within these by the highest CO_2 concentration. Seventeen of the 32 assessments found that a higher CO_2 concentration was significantly associated with a worsening of at least one outcome. Out of 18 assessments with SBS symptoms as outcomes (including studies with naturally ventilated buildings), 9 (50%) found a significantly higher prevalence of symptoms with higher CO_2 concentrations. Relative risks and odds ratios were reported in fewer CO_2 studies than ventilation rate studies. Relative risks for symptoms in the higher CO_2 groups ranged up to 1.85 (Sieber et al., 1998). An odds ratio of 8.0 for ln (CO_2 concentration) with non-specific symptoms was reported by NIOSH (1991). In addition, some studies found a dose-response relationship between outcomes and CO_2 concentration (Bright et al., 1992; Sohn et al., 1994). Restricting the review to findings of the ten studies reported in peer-reviewed articles eliminated most of the evidence for relationships.

The CO_2 concentrations in the studies varied considerably. Table 7 illustrates that the percentage of studies with a significant association between CO_2 concentration and SBS symptoms increased as higher concentrations of CO_2 were included in the study.

There was no clear threshold value for carbon dioxide concentration below which further reductions were not associated with further decreased SBS symptoms. Several studies (7 of 16) suggested that the risk of sick building symptoms continued to decrease with decreasing carbon dioxide concentrations below 800 ppm (corresponding to steady state ventilation rates of 11.6 Ls^{-1} per person). None of the assessments found an

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Table 7 Number of assessments with significant increase in SBS symptoms versus CO_2 concentrations included

CO_2 concentration (ppm)	600	1,000	1,400
Number of assessments including the CO_2 concentration indicated in row 1			
All assessments	16	7	4
Assessments with only mechanically-ventilated buildings	12	3	3
Number (proportion) of assessments with significant increase of SBS symptoms in higher CO_2 group			
All assessments	8 (50%)	4 (57%)	3 (75%)
Assessments with only mechanically-ventilated buildings	7 (58%)	3 (100%)	3 (100%)

increase of symptoms with decreasing carbon dioxide concentration.

Half of the 12 assessments with perceived air quality as outcome reported an association between air quality and CO_2 concentration and suggested that improvements in perceived air quality were associated with decreasing CO_2 concentration down to 500–600 ppm (corresponding to steady state ventilation rates of 34.7–20.8 Ls^{-1} per person).

While some studies used total SBS symptom scores, several studies tested for the association of several specific SBS symptoms (or symptom groups) with ventilation rates or carbon dioxide concentrations. We reviewed the data to determine if specific symptoms were most commonly associated significantly with ventilation rate or CO_2 concentration; however, we were not able to identify symptoms or symptom groups which were consistently associated with ventilation rate or CO_2 concentration. Significant associations with general symptoms including headache were reported in seven studies. Five studies reported significant associations with fatigue and significant associations with eye symptoms were reported in six studies. Significant associations with nasal symptoms were reported in four studies. Respiratory tract symptoms, which included several sub-groups such as throat symptoms, multiple lower respiratory symptoms, and breathing difficulties, were significantly associated with ventilation rates or CO_2 concentrations in four studies. Some studies reported significant associations with mucous membrane symptoms without specifying the exact end points.

Discussion

Overall Findings from Ventilation Studies

Summarizing findings of multiple studies based on statistical significance alone (as in the review by Mendell (1993b)) can be too conservative, ignoring consistent effects across studies and persuasive dose-response patterns within studies, when they lack statistical significance due to small study size. In particular, this strategy may systematically fail to detect real and important, yet small, differences in outcomes between relatively high ventilation rates. Our strategies here for synthesizing findings across studies overcomes some of the limitations in the previous review. This review contains a substantially larger number of studies, it includes for review only studies meeting specific quality criteria, and it considers two crucial additional aspects of study findings beyond statistical significance: estimated magnitude of the difference in outcome between ventilation rates (when available), and findings of dose-response relations between outcomes and ventilation rate.

Some remaining limitations inherent either in the review or the studies reviewed include: use of mean ventilation rates estimated from other reported numbers, less accurate ventilation measurements in some studies; and measurement of ventilation rates over large areas of buildings rather than more locally. Each of these limitations may introduce random error into ventilation rate estimates; however, all these errors unless systematically related to the outcome, would tend to obscure any existing relationships between ventilation and outcome. Also, dose-response relationships indicated by coefficients or slopes for continuous ventilation rate variables cannot be interpreted properly as showing significant association of ventilation with outcomes throughout the entire range of included ventilation rates.

The results of our review indicate that lower ventilation rates within the normally encountered range (2.5–30 Ls^{-1} per person) were significantly associated with both increased health effects and worsened perceived air quality. The reported or estimated relative risks were over 2.0 in five of 14 assessments and over 1.8 in nine assessments, indicating that changes in ventilation rates had a considerable influence on health outcomes and perceived air quality. SBS symptom prevalences at the higher reference ventilation levels were over 20% in half of the assessments. If the prevalence at the reference ventilation rates is 20%, a relative risk of 1.8 corresponds to a prevalence of 36% in the population with the lower ventilation rate. Thus, changes in ventilation rates potentially influence

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symptoms in a substantial proportion of the workforce.

The association of ventilation rates with health and perceived air quality (PAQ) was more consistent in assessments of buildings or spaces with lower ventilation rates. Such a finding was expected because changes in ventilation rates by a few Ls^{-1} per person will have a larger influence on indoor pollutant concentrations when the initial ventilation rate is low (because the percent change in ventilation rate is larger). Our findings are consistent with those of Mendell (1993b). Based on six studies, he reported a consistent association of higher SBS symptom prevalences with lower outside air ventilation rates below 10 Ls^{-1} per person. Of the 19 studies[5] meeting our selection criteria which included ventilation rates less than 10 Ls^{-1} per person, lower ventilation rates in 18 of these studies were significantly associated with a worsening of at least one health or PAQ outcome.[6] Thirty-one assessments in Table 4 included buildings or spaces with ventilation rates below 10 Ls^{-1} per person, and in 27 of these assessments lower ventilation rates were significantly associated with worsening of at least one health or PAQ outcome.

A significant association was not found in the cross-sectional study by Jaakkola et al. (1991a), which was conducted in a single large building. Several unusual factors were present: (1) the ventilation system was unusual with air supplied to the hallways and exhausted only from the perimeter offices; (2) smoking was allowed in both designated smoking areas and in private offices; (3) subjective symptom reporting on questionnaires may have been less reliable in this building because occupants were dissatisfied with having been moved to a new location and with management.

The experimental study of Jaakkola et al. (1994) also did not find variation in the recirculation rate from 0 to 70% (which affected the ventilation rate) to be associated with SBS symptoms. The measured outdoor air ventilation rates were 6 and 23 Ls^{-1} per person. The absence of an association may possibly be explained by one or several of the following factors: (1) there were only 72 subjects within two buildings; (2) occupants recorded their symptoms daily in a diary – a method not used in other studies; and (3) the buildings were not designed for the particularly high or low recirculation rates used in the experiments, which changed indoor pressure differences and may have caused an increased spread of indoor pollutants.

Jaakkola and Miettinen (1995) and Jaakkola et al. (1994) found a significant *increase* in prevalence of symptoms with increases in ventilation rates. These studies were performed in Finland in winter, when very low indoor humidities occur with high ventilation rates as in other cold climates. Due to low outdoor air temperatures, the water content (humidity ratio) outdoors is very low (below 1 g H_2O per kg dry air) during the winter time in Nordic countries. Low relative humidities also have been measured in buildings. Reinikainen et al. (1991) reported relative humidity of 10–20% in a Finnish office building, Sundell et al. (1994) reported a median value for relative humidity of 23.8% in 160 Swedish office buildings.

Nordström et al. (1995) studied symptoms and perceived air quality in eight hospitals and reported a significant increase in 2 of 13 symptoms with higher ventilation rates; however, the higher ventilation rates were associated with better perceived air quality. This contradictory result may possibly be a consequence of low relative humidity caused by increased ventilation rates. Low relative humidity increases the drying of mucous membranes, but improves the perceived air quality (Fang et al., 1998).

A cross-sectional study in Swedish schools (Wålinder et al., 1998) found objectively measured nasal patency and biomarkers for allergic reactions to be associated significantly with ventilation rate expressed as air changes per hour, but did not find these outcomes to be significantly associated with ventilation rate per person. This result suggests significant pollution from a source, unrelated to occupant density, in the school buildings, such as emissions from building materials or bioaerosol emissions from moisture damaged structures. Ventilation rates were low in this study, ranging on average from 1.1 to 9 Ls^{-1} per person.

We were not able to identify a no-effect threshold value of ventilation rate above which further increases had little or no effect on outcomes. The absence of such a threshold based on studies performed in a diverse set of buildings may be a consequence of the variation among buildings in pollutant sources and in many other factors that affect indoor air quality. Additionally, fewer studies have been performed with ventilation rates above ~15 L s^{-1} per person; thus, the available data may be insufficient for detection of a threshold.

Two studies with ventilation rates above 10 Ls^{-1} per person failed to detect an association of ventilation rate with health or PAQ outcomes. Wyon (1992) changed the ventilation rate to 70 and 140% of the design value in some sections of a hospital, and did not report statistically significant changes in the prevalence of SBS

[5] In this context, the research of Jaakkola (1991a) is counted as two studies, one experimental and one cross-sectional.

[6] In one study the outcome was a self-assessment of impaired mental functioning.

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symptoms. The number of subjects in these experimental groups was relatively small, 51 and 65. Also, hospitals have many sources of pollutants and a range of types of rooms with different ventilation rates. Thus, the measured ventilation rates may be a poorer surrogate for pollutant exposures in hospitals than in other buildings.

Menzies et al. (1993a) changed the ventilation rates in the range of 14–30 Ls^{-1} per person by adjusting the proportion of recirculated air in the supply air stream, and the prevalence of SBS symptoms did not change significantly after controlling for other factors. The reported ventilation rates were relatively high even during the low ventilation period, and the method based on CO_2 measurements is relatively inaccurate. Changes in high ventilation rates have a lower probability of substantially reducing adverse exposures. Ventilation rates were estimated from CO_2 measurements using a steady state mass balance, e.g., Equation 1, and this method of estimating ventilation rates is subject to several sources of error.

A dose-response relationship between ventilation rate and SBS symptoms was indicated in three studies including six different assessments (Groes, 1995; Sundell et al., 1994; Wu et al., 1996). A dose-response relationship between ventilation rate and PAQ outcomes was indicated in six studies assessments (Bluyssen et al., 1996; Groes, 1995; Nordström et al., 1995b; Palonen et al., 1990; Cochet et al., 1995; Zweers et al., 1990). In addition, Smedje et al. (1996) reported a dose-response relationship with subjectively assessed mental performance. Dose-response relationships increase the robustness of the findings, because they are less likely to be chance findings than associations involving only two ventilation rates.

We were not able to identify symptoms or symptom groups which were consistently associated with ventilation rate or CO_2 concentration. The inconsistency of the pattern of associated symptoms may be due to different causative agents in studied groups of buildings. As increased ventilation reduces the concentrations of many contaminants in the air, it is possible that the agents causing the symptoms have been different in different buildings.

The graphical presentation of results in Table 4 may over-emphasize the significance of the relationship of ventilation rates with SBS symptoms. The graphs indicate positive associations for all studies that found one or more symptoms to be significantly associated with ventilation rates. However, in most of these same studies several SBS symptoms were not significantly associated with ventilation rates, and in one case the relationship is based on one symptom out of nine (Ruotsalainen et al., 1994). However, as discussed below the overall findings are unlikely to be due to chance.

Overall Findings from CO_2 Studies

Results of the studies on the association of CO_2 concentrations with health and PAQ outcomes generally support the findings of an association of ventilation rates with outcomes; however, a larger proportion of the CO_2 studies, compared to ventilation rate studies, failed to find a significant association of CO_2 with health or perceived air quality outcomes; this was particularly true among the findings reported in peer-reviewed articles. We suspect that the less consistent findings of the CO_2 studies are due to the temporal variation in indoor CO_2 concentrations. CO_2 concentrations vary each day with time elapsed after the start of occupancy, even when the rate of outside air supply is stable. The timing of CO_2 measurements, and the CO_2 metrics used in the analyses (e.g., peak value, measured range), varied among the studies; thus, the measured CO_2 concentrations reflect the measurement time as well as the rate of air supply per occupant. More consistent results would be expected if all studies used either the peak or time-average indoor carbon dioxide concentration. The spatial variability in indoor CO_2 concentrations and the variability in the outdoor concentration have also not been addressed in many of the studies.

Only two studies reported CO_2 as the differences between indoor and outdoor CO_2 concentrations, a more reliable indicator of the ventilation rate than indoor concentration. Outdoor air concentrations were reported only in six studies out of 22; these data showed a significant variation in outdoor air concentration (275–549 ppm). The large range of reported values are also likely to reflect measurement errors.

The CO_2 values in the assessments depicted in Table 6 are subject to instrument measurement errors, failures to account for the variable outdoor carbon dioxide, and failure to standardize measurement locations and times. These factors may cause some of the CO_2 concentration ranges or means depicted in the graphic section of Table 6 to be in error by a significant amount, on the order of 100 ppm. We do not expect systematic errors (i.e., in one direction) in the CO_2 concentrations in relation to the associated health outcomes. Therefore, these inaccuracies will make it more difficult to detect actual associations and generally bias the estimated relative risks or odds ratios from these studies toward 1.0, causing observed associations with health outcomes to be smaller than the true associations.

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Chance Association

Most of the studies with SBS symptom outcomes assessed the associations of ventilation rates with specific or grouped SBS symptoms. With the typical criteria for statistical significance ($P<0.05$), there will be a statistically significant association due to chance found in about one out of 20 analyses where no real association exists. Thus, the following question arises: are the significant associations identified in these studies likely to be just chance associations? For several reasons, these findings appear not to be mere chance associations. First, when no actual relationship exists, chance negative associations are as probable as chance positive associations. However, there are only four reported significant negative associations (i.e., worse outcomes at higher ventilation rates), compared to 20 positive associations. Second, in every study with a reported significant association, the number of significant associations for different outcomes relative to the number of statistical tests performed exceeds the one in 20 expected by chance. Three assessments out of four with respiratory illnesses as the outcome found a statistically significant association in more than half of the statistical tests. 16 out of 20 assessments with SBS as the outcome found a statistically significant association in more than half of the statistical tests. In ten assessments with individually recorded SBS symptoms, five found an association with more than half of the recorded symptoms. These proportions are much higher than expected by chance. Third, as discussed above, there are several reported dose-response relationships, which are less likely to be caused by chance.

Confounding

Confounding can occur when some factor that varies in the study is associated with the independent variable (e.g., ventilation rate) and also affects the dependent variable (e.g., SBS symptom prevalence). The variability in the confounding factor can distort the measured relationship between the independent and dependent variable. Many, perhaps all, of the studies have not controlled for all of the important confounders. Confounding factors may have influenced associations found between ventilation and occupant outcomes in individual studies; however, confounding, which can increase or decrease the measured association, seems to be an unlikely explanation for the generally consistent findings of this review. The personal and work-related confounders (listed in Table 1), environmental tobacco smoke, and dusty surfaces are not likely to be associated in a consistent manner with ventilation rates. In addition, many studies have controlled for some of these potential confounders. The remaining potential confounders from Table 1 are sealed windows, type of ventilation system, humidification, building age, quantity of carpet or textile surfaces, air temperature, and air humidity. A brief discussion of the potential for confounding by each of these factors follows:

- Sealed windows, which are likely to be associated with lower ventilation rates in cross-sectional studies, might influence health or PAQ via some psychosocial or lighting-related mechanism (typically buildings with sealed windows have deeper bays and different illumination conditions). However, ventilation rates were associated with health symptoms in studies of buildings with all-openable windows (Sundell et al., 1994; Jaakkola and Miettinen, 1995; Palonen et al., 1990; Ruotsalainen et al., 1994; Smedje et al., 1996) and with all-sealed windows (Gamble et al., 1986; Milton et al., 1999; Wu et al., 1996). Also, window characteristics were controlled in the experimental studies. Overall, a high level of confounding with window type seems unlikely.
- The type of ventilation system may be associated with ventilation rate in the cross-sectional studies and also associated with the risk of microbiological or other pollutant sources in the ventilation systems that cause symptoms. However, such confounding would be an unlikely source of the observed dose-response relationships and such confounding did not occur in the experimental studies. Additionally, naturally ventilated buildings, although associated with lower symptom prevalence, appear more likely to have lower ventilation rates (Bluyssen et al., 1996; Sundell et al., 1994). Three large studies (Bluyssen et al., 1996; Jaakkola and Miettinen, 1995; Sundell et al., 1994) which reported significant associations with ventilation included buildings with several ventilation and air conditioning system types.
- Humidification systems have been linked with SBS symptoms, and humidification is more common in cold dry climates where there is an increased incentive to save energy by reducing ventilation. However, several of the cross-sectional studies with significant associations did not include humidified buildings (Jaakkola et al., 1991 a, b; Jaakkola et al., 1995; Palonen et al., 1990; Ruotsalainen et al., 1994; Smedje et al., 1996). Significant associations were also reported in studies limited to humidified buildings (Milton et al., 1999) and studies with both non-humidified and humidified buildings (Bluyssen et al., 1996; Sundell et al., 1994). The latter studies controlled for humidification in the data analysis. Fur-

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thermore, humidification would not confound experimental ventilation studies.

- Carpets and textile surfaces have been associated with SBS symptoms and carpets and textiles may be more common in newer buildings that may have lower ventilation rates. Such confounding seems an unlikely explanation for the overall findings because some cross-sectional studies and all experimental studies controlled for carpets and other "fleecy" surfaces. Also, the association of fleecy surfaces with ventilation rate is weak, and possibly non-existent.
- Increased air temperatures have been associated with an increased prevalence of SBS symptoms and worsened perceptions of indoor air quality. However, there is no overriding reason to expect systematically higher temperatures with lower ventilation rates. Also, some studies have controlled for temperature in the data analyses.
- Humidities that are particularly low have been associated with increased skin and mucous membrane symptoms in a few studies. These particularly low humidities are more likely to be associated with high ventilation rates in cold climates than with low ventilation rates. Higher humidities have been linked with worsened PAQ in laboratory research and higher humidity may be associated with decreased ventilation. Thus, humidity could be an uncontrolled confounder in some studies. However, in field studies, higher humidity has not been consistently or strongly associated with increased SBS symptoms.
- Building age may be a surrogate for a number of risk factors for SBS symptoms and poorer PAQ. The association of age with ventilation rate is based on the expectation that more recent concerns about energy use have resulted in less leaky building envelopes and ventilation system designs with lower ventilation rates. However, the ventilation system design does not necessarily determine the ventilation rate. For many designs, with recirculation of return air the ventilation rates can be set within a wide range. Also, there is no confirmation of a strong association of building age with ventilation rate. The age of buildings may be related to the types and strengths of indoor pollutant sources. Older buildings may have a higher probability of microbiological contamination. Newer buildings, particularly those that are very new, may have more or stronger sources of volatile organic compounds emitted by building materials. However, excluding very new buildings, the association of volatile organic compounds (VOCs) with age is likely to be weak because buildings are periodically refurbished. Also the emissions of VOCs from consumer products and equipment may not differ substantially between newer and older buildings. Overall, a high level of confounding with building age seems unlikely.

Other Sources of Bias

A bias common to most or all studies seems improbable as an explanation of our overall findings. There is no reason to expect that the building selection process causes a relevant bias, since the investigators do not know the ventilation rates prior to making measurements. Building occupants are almost always unaware of ventilation rates; thus, symptom reporting should be unbiased by any expectations regarding the effects of ventilation. There are many sources of error in ventilation rate measurements, but the direction of the errors should be independent of the building ventilation rate and these errors would reduce the ability to detect real relationships. Finally, we have no reason to expect that researchers have intentionally or unintentionally caused bias during their data analyses. Publication bias remains a possibility, since studies finding significant associations are more often published than those finding no associations; however, lack of associations in this research area are considered of importance and are readily publishable (Menzies et al., 1993a; Wyon et al., 1992).

Reported ventilation rates in the studies reviewed are likely to be biased downward because most of the data are based on air flow rate measurements, which will not account fully for air infiltration. Thus the actual ventilation rates are in most cases higher than reported and shown in Tables 3 and 4. Simultaneous flow rate and tracer gas measurements by Nagda et al. (1990, 1991) and Persily et al. (1987) showed almost 50% higher ventilation rates with tracer gas measurements than with air flow rate measurements in buildings with very low ventilation rates. The mechanical supply of outdoor air often does not exceed the rate of mechanical exhaust airflow by an amount sufficient to pressurize the building and prevent air infiltration because the building envelopes are leaky (Persily et al., 1987). The likelihood of such a systematic measurement bias in most studies reviewed, and the generally consistent associations between ventilation rates and symptoms, suggests that true ventilation rates even higher than those found in this review are associated with improved occupant outcomes. The errors in CO_2 determinations, from instrument errors, failure to account for outdoor CO_2, etc., will lead to random misclassification of buildings

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as having reported values of CO_2 that are higher or lower than actual values. Such a random misclassification will make it more difficult to detect actual associations between CO_2 and health outcomes and will tend to bias the odds ratios or relative risks towards no effect.

Relative Risks and Excess Risk

The reviewed studies reported relative risks of 1.5 to 4.7 for respiratory illnesses and 1.1 to 6 for sick building symptoms. The most representative study data from US office buildings (Brightman et al., 1999) found that 20% and 25% of office workers reported that they experienced work-related upper-respiratory or eye symptoms, respectively, at least once per week. Typical prevalences of individual sick building symptoms in European buildings are of the same magnitude, ranging from 7 to 32% (Bluyssen et al., 1996). The results of Jaakkola (1995) indicate that each 1 Ls^{-1} per person change in ventilation rate between 0 and 25 Ls^{-1} per person (which includes most indoor environments) is associated with a relative risk of 1.1 for experiencing symptoms. Assuming this relationship is causal, we can estimate that a 5 Ls^{-1} per person increase in ventilation rate in US office buildings would reduce the proportion of occupants with frequent upper respiratory symptoms (as defined above) from 25 to 16%. The corresponding estimated reduction in prevalence of eye symptoms is from 22 to 14%. Similarly, a 5 Ls^{-1} per person decrease in ventilation rate would increase the proportion of occupants with frequent upper respiratory symptoms from 25 to 40%, with an increase for eye symptoms of similar magnitude.

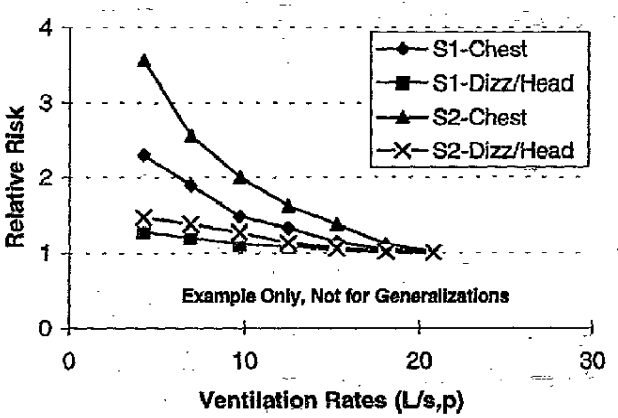

Fig. 1 An example of relative risk plots for two kinds of symptoms (chest=rate of chest distress and dizz/head=rate of dizziness and headache) at various lowered ventilation rates relative to 21 Ls^{-1} in two buildings (S1 and S2). This figure does not present a generic relation even though it is derived from real data (Wu, 1996)

Published discussions of ventilation rates and health have generally not discussed how scientific findings could be used to determine health-protective ventilation rates. There is a tradition among indoor environment practitioners that conditions are acceptable which dissatisfy no more than 20% of the population. This is presumably based on customs in the field of thermal comfort. Health risk assessments, by contrast, usually assess excess risk of disease relative to a maximum acceptable excess risk above a background (unexposed) level, where the acceptable excess risk depends on the severity of the health effect. Excess lifetime risks considered acceptable may range from 10^{-6} or 10^{-5} for potentially fatal outcomes such as cancer, to 10^{-3} for less serious outcomes. Applying this strategy to effects of ventilation rate would involve determining baseline levels of health effects, and deciding what additional risk was acceptable.

Many studies report the association of ventilation rates with health outcomes only as a model coefficient or report that a significant dose-response was found within that range. These findings help corroborate that a relationship exists, but are not easily used in making decisions about recommended ventilation rates. By assuming a linear relationship throughout the ventilation rates included, they provide no information on whether the relationship in fact holds equally throughout this range. Reporting formats that distinguish the magnitude of outcome differences at multiple specific ventilation levels would be more usable, both in future studies, and in recalculations from previous studies. One format particularly useful for public health decision making would estimate risks, relative to background levels (e.g., high ventilation rates with minimal exposure to indoor pollutants), for various levels of the risk factor (e.g., lower ventilation rates with resulting higher concentrations of indoor pollutants).

Figure 1 provides an example of relative risk plots for two kinds of symptoms in relation to various lowered ventilation rates relative to 21 Ls^{-1} in two buildings. The purpose of this plot is to illustrate how data on the risks of low ventilation rates could be presented for public health purposes. The excess risk for a symptom, at each ventilation rate, would be the relative risk at that ventilation rate minus 1. This figure does not present a generic relation even though it is derived from real data points (unadjusted relative risks from Wu (1996)). These results also do not show that ventilation rates above 21 L s^{-1} per person would not further reduse risks – the ventilation rate 21 Ls^{-1} per person was used as the reference value in the figure because it was the highest ventilation rate included in the study.

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Other Issues

The ventilation rate in most studies reviewed was expressed in Ls^{-1} per person. The ventilation rate can be converted to Ls^{-1} per square meter of floor area in most but not all of these studies. The floor space per occupant was in the range of 15–25 m^2 per person in most of the office buildings except in the Asian study (Wu, 1996) which had much less space per person (3–4 m^2 per person). When the conversion to Ls^{-1} per m^2 was made, ventilation rates below 1 $Ls^{-1}m^{-2}$ appeared to be associated with an increased risk of adverse health effects and poor PAQ. With the available data, we could not determine if the outcomes were more strongly and consistently associated with ventilation per person or ventilation per unit floor area.

This review suggests that in many cases increases in ventilation rates are associated with improved occupant health; however, increases in ventilation rates will also often increase building energy consumption and the initial costs of HVAC systems and supporting utility infrastructure. The study data in this review indicate substantial variation in ventilation rates both within and among buildings, consistent with earlier findings (Fisk et al., 1992; Lagus Applied Technologies, 1995; Teijonsalo et al., 1996). The large range of ventilation rates within buildings suggests an opportunity to improve health and PAQ through better balancing and control of air flows within buildings. Ventilation rates may be increased in rooms with unusually low ventilation rates and simultaneously decreased in rooms with unusually high ventilation rates. Due to the dose-response relationships evident from this review, the average level of SBS symptoms and PAQ should be improved without increasing the total ventilation rate of the building or the associated energy use. There is an analogous opportunity to alleviate symptoms and improve PAQ in the overall building stock without increasing energy consumption, by increasing ventilation rates in buildings with low ventilation rates and decreasing ventilation rates in buildings with high ventilation rates. It seems quite possible that better ventilation control and balancing could simultaneously improve health and PAQ outcomes while saving energy.

In a European study, buildings with lower energy consumption also had a lower rate of building-related symptoms (Bluyssen et al., 1996; Roulet et al., 1995). This finding suggests that well-designed buildings which are operated by qualified, well-trained personnel who understand both the requirements for good indoor air quality and energy efficiency can have healthy environments and maintain energy efficiency.

Indoor air quality is affected by many factors other than ventilation rates. The quality of supply air is important as well as the spatial and temporal distribution of fresh air. Several strategies for ventilation exist, such as displacement ventilation or ventilation with energy recovery, which improve indoor air quality without increasing energy consumption. Additionally, reductions in indoor pollutant sources[7] are often the most effective and energy efficient means of improving indoor air quality. In the best cases, improvements in indoor air quality and energy savings are achieved simultaneously. Some of these technologies and strategies are discussed in Seppänen (1999); ECA 17 (1998); Hall et al. (1998) and IPMVP IEQ Committee (1999).

In addition to energy savings and improved health, improved control of ventilation rates and other measures that improve indoor air quality in commercial buildings are a likely source of productivity gains. The potential productivity gains from reduced respiratory illnesses and SBS symptoms have been discussed in detail by Fisk and Rosenfeld (1997, 1998) and Seppänen and Palonen (1998). The primary sources of productivity gains are reduced health care costs, reduced absence from work, and increases in the performance of workers while at work. These costs and the financial values of the reduced absences and performance increases are of the same magnitude as the total energy cost of the buildings, much larger than the costs of energy for ventilation (Seppänen and Palonen, 1998; Seppänen, 1999).

Conclusions and Implications

The complex relationship between ventilation rate and indoor air quality greatly complicates research on the associations of ventilation rates with health outcomes and perceived air quality. Many of the studies have failed to control for important potential confounders or have incompletely characterized the study buildings and study methods. The difficulties and inaccuracies in ventilation rate measurements have also served as a barrier to this area of research.

Almost all the studies included in this review found that ventilation rates below 10 Ls^{-1} per person were associated with a significantly worse prevalence or value of one or more health or perceived air quality outcomes. Most of these studies have been conducted in office buildings. Available studies further show that increases in ventilation rates above 10 Ls^{-1} per person, up to approximately 20 Ls^{-1} per person, are sometimes associated with a significant decrease in the prevalence of SBS symptoms or with improvements in perceived

[7] However, we do not yet have substantial data linking specific reductions in pollutant sources with improved health outcomes.

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air quality. Data from multiple studies also indicate a dose-response relationship between ventilation rates and health and perceived air quality outcomes, up to approximately 25 Ls^{-1} per person; however, available data are not sufficient to quantify an average dose-response relationship. The less consistent findings for relationships in the range above 10 Ls^{-1} per person are compatible with the prediction that benefits per unit increase in ventilation would be likely to diminish at higher ventilation rates and, thus, be more difficult to detect epidemiologically. Only five studies were conducted in hot humid climates; thus, the results of this review apply primarily to moderate and cool climates.

Based on these results, we conclude that in office buildings or similar spaces constructed using current building practices, increases in ventilation rate in the range between 0 and 10 Ls^{-1} per person will, on average, significantly reduce occupant symptoms and improve perceived air quality. Increases in ventilation rate above 10 Ls^{-1} per person up to 20 Ls^{-1} per person may further reduce symptoms and improve air quality, although these benefits are currently less certain based on available data. No threshold for effects is evident at 10 Ls^{-1} per person or at any other specific ventilation rate. As ventilation rates increase, benefits gained for occupants per additional unit of ventilation are likely to decrease in magnitude and to require larger studies for convincing demonstration. Benefits which have yet to be consistently demonstrated in this way (e.g., for ventilation rates above 10 Ls^{-1} per person) may still be of substantial public health importance. Ventilation standards thus may need to periodically revisit the available evidence for occupant benefits at particular ventilation rates, and the magnitude of these benefits, weighed against the current incremental costs of increasing ventilation. This process would be new, as minimum ventilation rates in existing codes and standards do not substantially reflect health data such as is reviewed here.

Furthermore, buildings in practice often fail to deliver even the minimum ventilation rates required by current or previous building codes (e.g., of the 15 cross-sectional surveys included in Table 2, 10 surveys include buildings with ventilation rates below 2.5 Ls^{-1} per person). These low ventilation rates usually do not violate building codes and standards, which generally specify minimum rates for ventilation system design but not for system operation. New or revised building codes and standards may need to specify minimum ventilation rates during building occupancy to maintain acceptable levels of occupant health and satisfaction. Buildings with economizer cycle control systems have a minimum ventilation rate and increase the rate of ventilation above this minimum during mild weather. Changing the set point for minimum ventilation rate in these buildings will influence health symptoms during periods of low ventilation when the control system reduces the ventilation rates close to the minimum.

Limitations in existing data make it essential that future studies better assess health and PAQ changes in the ventilation rate range between 10 and 25 Ls^{-1} per person. Future research should be based on well-controlled cross-sectional studies or well-designed blinded and controlled experiments. The most effective studies will include high quality measurements of ventilation rates, ample study size and power to detect effects considered of public health importance, and if possible, improved measures of adverse occupant outcomes; e.g., more sensitive or more objective assessment tools. Future research should also assess the associations of health outcomes with ventilation rates per unit floor area and place a greater emphasis on buildings that are not offices.

In addition to new studies of ventilation effects on occupants, we also need studies to specify the causative agents of adverse health outcomes. The most effective strategies to improve indoor air quality (e.g., source removal) cannot be specified before the agents and their sources are known. When this information is available the ventilation rates necessary to control exposures can be calculated using Equation 1, and rational decisions made between effectiveness of source control and adjustment of ventilation.

Because increases in ventilation may increase building energy consumption, research is also needed to identify practical methods of decreasing minimum ventilation requirements by reducing pollutant emissions from buildings and building air-handling systems. Methods to increase ventilation rates without increasing energy consumption, or to increase the effectiveness of ventilation in controlling pollutant exposures, should also be investigated.

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